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The opinion of the U.S. Court of Appeals for the Federal Circuit (App., *infra*, A1) was published on February 19, 2010. *See In Re Sami Chemicals and Extracts, Ltd.*, 367 Fed. App'x 150 (Fed. Cir. 2010). The order of the U.S. Court of Appeals for the Federal Circuit denying panel rehearing and denying rehearing *en banc* (App., infra, A39-A40) was published on May 4, 2010.

The opinion of the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office (App., infra, A2-A25) is reported at *Ex Parte Sami Chemicals and Extracts, Ltd.*, Appeal 2007-3482, 2007 WL 4366677 (Bd. Pat. App. & Interf. Dec. 13, 2007).

The opinion of the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office denying a request for rehearing (App., infra, A26-A38) is reported at *Ex Parte Sami Chemicals and Extracts, Ltd.*, Appeal 2007-3482, 2009 WL 247849 (Bd. Pat. App. & Interf. Feb. 2, 2009).

JURISDICTION

The judgment of the U.S. Court of Appeals for the Federal Circuit was entered on February 19, 2010. Petitioner's request for rehearing was denied on April 27, 2010. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

"A person shall be entitled to a patent unless – the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States." 35 U.S.C. § 102(b).

"A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made." 35 U.S.C. § 103(a).

"The patent owner involved in a reexamination proceeding under this chapter may appeal under the provisions of section 134 of this title, and may seek court review under the provisions of sections 141 to 145 of this title, with respect to any decision adverse to the patentability of any original or proposed amended or new claim of the patent." 35 U.S.C. § 306.

REGULATION INVOLVED

New ground of rejection. Should the Board have a basis not involved in the appeal for rejecting any pending claim, it may enter a new ground of rejection. A new ground of rejection shall be

considered an interlocutory order and shall not be considered a final decision. If the Board enters a new ground of rejection, within two months appellant must exercise one of the following two options with respect to the new ground of rejection to avoid dismissal of the appeal as to any claim subject to the new ground of rejection:

(1) *Reopen prosecution.* Submit an amendment of the claims subject to a new ground of rejection or new evidence relating to the new ground of rejection or both, and request that the matter be reconsidered by the examiner. The application or reexamination proceeding on appeal will be remanded to the examiner. A new ground of rejection by the Board is binding on the examiner unless, in the opinion of the examiner, the amendment or new evidence overcomes the new ground of rejection. In the event the examiner maintains the new ground of rejection, appellant may again appeal to the Board.

(2) *Request for rehearing.* Submit a request for rehearing pursuant to §41.52 of this sub-part relying on the Record. 37 C.F.R. § 41.50(d).

INTRODUCTION

This case raises fundamental questions regarding the right to a full and fair hearing for a patent holder pursuing reexamination of its patent.

Reexamination of a patent in the U.S. Patent and Trademark Office (PTO) may be sought in order to determine if a patent is valid over one or more patents or printed publications submitted with the request for reexamination. If the PTO determines

that a substantial new question of patentability exists, the request for reexamination is granted. The patent holder is then given an opportunity to respond to rejections by presenting arguments, amending the claims, and/or presenting new claims.

If the patent holder is unable to convince the patent examiner of the patentability of the claims during the reexamination process, the patent holder may appeal the rejections to the Board of Appeals and Patent Interferences (Board).

The Board reviews the appealed rejections, and has the authority to issue new rejections not previously involved in the appeal when it renders its decision. However, when the Board issues a new rejection, the "new ground of rejection shall be considered an interlocutory order and shall not be considered a final decision." 37 C.F.R. § 41.50(d). If a new rejection is issued, the patent holder may request a rehearing or reopening of prosecution in order to address the new rejection and avoid dismissal of the appeal as to the claims subject to the new ground of rejection. *See* 37 C.F.R. § 41.50(d). These options are necessary to avoid depriving the patent holder of its patent without a full opportunity to respond to the basis for the rejection of its claims. *See* 35 U.S.C. § 306.

In the case of an appealed reexamination proceeding, premature dismissal of the appeal results in issuance of a reexamination certificate in which the newly-rejected claims are cancelled. This deprives the patent holder of the right to its valuable intellectual property.

In this case, Petitioner pursued reexamination of its U.S. Patent No. 5,804,596 (the '596 patent) in U.S. Reexamination Application No. 90/007,327 (the '327 application). Petitioner appealed the final rejections of all claims of the patent to the Board. The Board upheld the rejections in its Decision on Appeal. App., *infra*, A2-A25. However, the Board used a new basis for rejecting the claims, relying on a new claim construction formulated using a previously-uncited dictionary definition. App., *infra*, A9-A10.

The Board denied Petitioner's requests for rehearing or reopening of prosecution following issuance of the new ground of rejection. App., *infra*, A26-A38. The Board's decision was timely appealed to the Federal Circuit, which affirmed the Board's decision without comment. App., *infra*, A1.

The Court should grant this petition in order to instruct the Federal Circuit and the Board that patent holders have a fundamental right to fully and fairly address claim rejections before reexamination decisions adverse to their patents are made final.

STATEMENT OF THE CASE

A. The '596 Patent

The '596 patent is directed to the use of forskohlin, a diterpene compound extracted from the *Coleus forskohlii* plant, to increase lean body mass. App., *infra*, A50-68.

The human body is composed of body fat and lean body mass. Lean body mass includes muscles, vital organs, bones, connective and other non-fatty

tissues in the body, and body water. The body's metabolic rate is directly proportional to lean body mass. Therefore, lean body mass is important in developing an intelligent weight-loss strategy. App., *infra*, A53.

Most weight-loss compositions known in the art are designed to decrease the amount of body fat by decreasing appetite for food, decreasing food absorption, slowing down the rate of fatty acid synthesis within the body, or increasing the rate of catabolism of fatty acids. App., *infra*, A52. These regimens to decrease body fat often contribute to the catabolic wasting of lean body mass. Increased lean body mass regulates body metabolism and helps in losing weight. Conversely, diminished lean body mass slows down body metabolism and results in difficulties in maintaining an appropriate, healthy body weight. App., *infra*, A53-A54.

In the prior art, it was known that forskohlin stimulates cyclic AMP (cAMP) and lipolysis in isolated fat tissues. App., *infra*, A54-A55. The '596 patentees discuss this state of the art in detail in the "Background of the Invention" section of the '596 patent. App., *infra*, A54-A55. The three references noted in the patent specification (i.e., Hoffman et al., *Horm. Metabol. Res.* 19, 358-360, 1987; Allen et al., *J. Pharmacol. Experim. Ther.* 238, 659-664, 1986; and Allen et al., *J. Pharmacol. Experim. Ther.* 244, 852-858, 1988), were considered by the examiner during the initial prosecution of the '596 patent, and are listed on the front cover of the patent. App., *infra*, A50-A51. After the '596 patentees discuss this prior art, the paragraph ends with the following statement: "However, the use of forskohlin for the

promotion of lean body mass has not been reported." App., *infra*, A55.

The patentees theorized regarding the biological mechanisms that may be responsible for how the invention works:

> Without being bound by any theory, the present inventors believe that the invention increases the lean body mass by [activating various biological mechanisms]. Thus, the formation of lean body mass is promoted. App., *infra*, A57-A58.

The appealed claims of the present application are specifically directed to the use of forskohlin described above. Independent claim 1 reads as follows:

> 1. A method of promoting lean body mass in a human individual in need thereof, comprising administering to the individual a lean body mass promoting effective amount of forskohlin. App., *infra*, A66.

None of the cited references discloses or suggests the method of claim 1. Indeed, each of the references discloses the known prior-art use of forskohlin to stimulate lipolysis and shuttle fat from the cells, which is different from ***promoting*** lean mass.

B. The Reexamination Proceedings

During reexamination of the '596 patent, the examiner, *inter alia*, rejected claim 1 and several dependent claims under 35 U.S.C. § 102(b) as being anticipated by Kazuo or Greenway. App., *infra*, A3-A4. The examiner also rejected all claims under 35 U.S.C. § 103(a) as being obvious over Kazuo, stating that any differences between the claims and the reference would have been obvious. App., *infra*, A4.

The Board affirmed the examiner's prior-art rejections. App., *infra*, A18, A23-A24. In doing so, the Board conducted a claim-construction analysis in which it provided new interpretations of the claims not previously presented during prosecution. App., *infra*, A8-A12. For the terms "promoting" and "human individual in need thereof," the Board used the following construction:

> Therefore, ***we broadly interpret "promoting" lean body mass***, consistent with the '596 specification, ***as "furthering or bringing about" lean body mass. "Promoting" lean body mass is not limited solely to "increasing" lean body mass***, but also encompasses furthering lean body mass by maintaining lean body mass; reducing body fat relative to lean body mass; inducing cAMP mechanisms; and, improving absorption of nutrients and their preferential incorporation into lean body mass. App., infra, A10, emphasis added.
>
> . . . .

> [W]e broadly construe a "human individual in need thereof" to be an individual wanting more lean body mass or wanting to lessen or prevent accumulation of fat (adipose tissue). App., *infra*, A12.[1]

The Board's construction of these terms was inconsistent with the manner in which the terms had been interpreted during reexamination before the examiner. Indeed, the Board's interpretation of the term "promoting" relied on a newly-cited dictionary definition that the Board attached to the Decision on Appeal.[2] App., *infra*, A100. Armed with these new claim interpretations, the Board affirmed the final rejections. In its findings, the Board relied on its new interpretation of the claims and the newly-cited dictionary excerpts. For example, in applying the Kazuo reference to the claimed invention, the Board noted that:

---

[1] The Board's construction of "human individual in need thereof" did not differentiate between the way these terms were used in claim 1 and non-appealed claim 5: "The claims require that the method be performed on a 'human individual in need thereof' and that the method be used for 'promoting lean body mass' (claim 1) or for 'shifting the proportion between lean body mass and adipose tissue in favor of lean body mass' (claim 5)." Thus, it is unclear whether the Board's construction of "human individual in need thereof" applies solely to claim 1.

[2] The Board held that: "The ordinary meaning of 'promoting' is, in relevant part, to further or help bring into being (see e.g., Merriam-Webster's COLLEGIATE DICTIONARY, tenth edition (1998) at 933 (copy attached))." App., *infra*, A9.

> Experiment II of Kazuo is directed to prevention of obesity, i.e., preventing accumulation of excess body fat (see e.g., Merriam-Webster's COLLEGIATE DICTIONARY, tenth edition (1998) at 801 (copy attached)). App., *infra*, A14 (internal citations omitted).
>
> . . . [L]ean body mass may be "promoted" by various means including reducing body fat relative to lean body mass and inducing cAMP mechanisms (which Kazuo recognizes forskohlin does). App., *infra*, A17.
>
> The volunteers participating in Experiment II [of Kazuo] were administered an amount of forskohlin effective for the prevention of obesity and are "humans in need thereof" by virtue of wanting to prevent fat accumulation. App., *infra*, A14 (internal citations omitted).

Petitioner filed a Request for Rehearing, arguing that because the Board relied on a new claim construction to affirm the Examiner's rejections, the Board had *de facto* issued a new ground of rejection in the Decision on Appeal. Petitioner submitted that it was entitled to a full and fair opportunity to respond to the new ground of rejection, and requested reopening of prosecution under 37 C.F.R. § 41.50(b)(1) and remand of the case to the Examiner. App., A27. *Ex parte Felder*, No. APL 2008-3387, 2008 WL 3991998 (Bd. Pat. App. & Interf. Aug. 27, 2008) supports the proposition that a

rejection based on a new claim interpretation is a new ground of rejection. *Ex parte Felder* also addressed a situation where the new rejection was based on the same prior-art reference, as in the present case. *Id.* Petitioner submitted that reopening of prosecution was appropriate to allow it to amend the claims in a manner consistent with the new interpretation adopted by the Board. App., *infra*, A27.

The Board denied Petitioner's Request for Rehearing. App., *infra*, A38. The Board denied that its affirmance of the Examiner's rejections was a new ground of rejection. App., *infra*, A37. The Board held that the examiner's interpretation of the term "promoting" during *ex parte* reexamination was consistent with the Board's interpretation of the term in the Decision on Appeal. The Board stated that:

> [T]he fact that the Examiner rejected claims 1 and 5 together under § 102(b) suggests that she deemed a method of promoting lean body mass (claim 1) and a method of shifting the proportion between lean body mass and adipose tissue in favor of lean body mass (claim 5) to be the same method discussed in the prior art, i.e., Kazuo and the Greenway references. Moreover, the Examiner indicates in her discussion of the Greenway references that body mass is the sum of lean body mass plus body fat and, thus, reduction of fat would translate into promotion of lean body mass. Thus, it reasonably appears

> the Examiner broadly interpreted 'promoting' lean body mass to not only include increasing lean body mass as argued by Appellant, but also to include reducing body fat relative to lean body mass. App., *infra*, A37.

Petitioner timely appealed the Decision on Rehearing to the Federal Circuit, which had jurisdiction pursuant to 28 U.S.C. § 1295(4)(A).

C. Proceedings Before the Federal Circuit

The Federal Circuit failed to fully consider Petitioner's arguments, and instead issued a non-precedential, one page opinion affirming the Board's decision without comment. App., *infra*, A1.

Petitioner requested reconsideration in its Petitions for Panel Rehearing and *En Banc* Rehearing, to no avail. App., *infra*, A39-A40.

Petitioner has therefore timely appealed the opinion of the Federal Circuit to this Court.

REASONS THIS PETITION SHOULD BE GRANTED

I. POINTS OF FACT AND LAW WERE OVERLOOKED AND/OR MISAPPREHENDED BY THE FEDERAL CIRCUIT

Petitioner respectfully submits that the Federal Circuit misapprehended the following points of law and fact in affirming the decision of the Board finding claims 1, 9, 31, and 33 of U.S. Reexamination Application No. 90/007,327 ("the '327 application") anticipated under 35 U.S.C. § 102(b) in view of JP 6-133731 ("Kazuo"), finding claims 1, 11, 31, and 33 of the '327 application anticipated under 35 U.S.C. § 102(b) in view of Greenway et al., *Clin. Ther.* 9(6):663-669, 1987 ("Greenway III") or Greenway et al., *Obesity Res.* 3(Suppl):561S-568S, 1995 ("Greenway IV"), and finding claims 1-4, 9, 11, 13, 15-17, 19, 21, 23, 25, 27, 29, 31, and 33 of the '327 application obvious under 35 U.S.C. § 103(a) in view of Kazuo.[3]

A. By adopting a new, legally-incorrect claim construction for the term "promoting," the Board effectively issued new rejections. The Board failed to comply with the provisions of 37 C.F.R. § 41.50(d) when it refused to remand the '327 application to the Examiner for further proceedings,

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[3] Claims 1-4, 9, 11, 13, 15-17, 19, 21, 23, 25, 27, 29, 31, and 33 of the '327 application are on Appeal. Claim 1 is the only independent claim on appeal. Therefore, for ease of reference, Petitioner restricts its arguments to claim 1.

and the Federal Circuit erred when it failed to order such a remand. Petitioner requests that this Court order that the '327 application be remanded to the PTO for further proceedings.

B. There is no evidence in the record to support at least two of the claim constructions that were affirmed by the Federal Circuit. In particular, there was no evidence in the record to support the Board's conclusions that:

> 1. The term "effective amount" should be construed to mean an amount of forskohlin that promotes lean body mass, where the effectiveness may be systemic ***or localized***; and
>
> 2. The term "promoting" should be construed to mean increasing lean body mass, ***furthering lean body mass by maintaining lean body mass***, reducing body fat relative to lean body mass, ***inducing cAMP mechanisms, and improving absorption of nutrients and their preferential incorporation into lean body mass***.

Both of these errors are not merely errors in evaluating evidence justifying or detracting from the respective conclusion. Rather, there is literally no evidence in the record to support these claim constructions.

C. There is no evidence in the record to support at least two key findings of fact made as a result of the improper claim constructions adopted

for "promoting" and "effective amount." In particular, there is no evidence in the record to support the Federal Circuit's adoption of the Board's findings that:

> 1. Kazuo allegedly discloses administering an effective amount of forskohlin that promotes lean body mass; and
>
> 2. Greenway III and Greenway IV allegedly disclose administering an effective amount of forskohlin that promotes lean body mass.

D. The Board relied upon each of the above-identified claim constructions and findings of fact in reaching its conclusions regarding anticipation and obviousness. Because the conclusions of anticipation and obviousness affirmed by the Federal Circuit were based on legally-incorrect claim constructions, and factual findings not supported by substantial evidence, they should be reversed.

II. ARGUMENT IN SUPPORT OF REMANDING THE '327 APPLICATION FOR FURTHER PROCEEDINGS

A. Standard of Review and Applicable Law

A determination that a claim is anticipated under 35 U.S.C. § 102(b) involves two analytical steps. First, the Board must interpret the claim language, where necessary. This is a question of law that this Court reviews *de novo*. *Cybor Corp. v. FAS*

Techs., Inc., 138 F.3d 1448, 1456 (Fed. Cir. 1998); *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1355 (Fed. Cir. 2000). Secondly, the Board must compare the construed claim to a prior-art reference, and make factual findings that "each and every limitation is found either expressly or inherently in [that] single prior art reference." *Celeritas Techs., Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998).

Several basic factual inquiries must be made to determine the obviousness or non-obviousness of patent claims under 35 U.S.C. § 103. These factual inquiries are set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 86 (1966):

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or non-obviousness of the subject matter is determined.

Id. at 17.

The Board's factual findings are reviewed for substantial evidence. *In re Gartside*, 203 F.3d 1305, 1313 (Fed. Cir. 2000). Substantial evidence is such relevant evidence as a reasonable mind might accept to support the finding, taking into account evidence that both justifies and detracts from the finding. *See id.* at 1312 (citing *Consolidated Edison Co. v. NLRB*, 305 U.S. 197, 229-30 (1938)). Although the substantial evidence standard of review is a

deferential standard, the Board must still point to some concrete evidence in the record to support its findings of fact. *In re Zurko*, 258 F.3d 1379, 1386 (Fed. Cir. 2001) ("To hold otherwise would render the process of appellate review for substantial evidence on the record a meaningless exercise.") (citing *Baltimore & Ohio R.R. Co. v. Aberdeen & Rockfish R.R. Co.*, 393 U.S. 87, 91-92 (1968)). This Court has emphasized the "importance of not simply rubber-stamping agency factfinding." *Dickinson v. Zurko*, 527 U.S. 150, 162 (1999) (citing *Universal Camera Corp. v. NLRB*, 340 U.S. 474, 490 (1951)).

B. There is No Support for the Federal Circuit's Affirmance of the Constructions of the Terms "Effective Amount" and "Promoting"

By affirming the Board's claim constructions, the Federal Circuit issued an opinion that was inconsistent with prior Federal Circuit precedent. Although the Board is permitted to construe claims to have their broadest reasonable interpretation consistent with the specification, in this case the Board violated that tenet and adopted definitions contrary to the specification. Accordingly, this Court should reverse the Federal Circuit's affirmance of the Board's constructions of the terms "effective amount" and "promoting" because they are legally incorrect and not based on any evidence in the record. *See In re Trans Tex. Holdings Corp.*, 498 F.3d 1290 (Fed. Cir. 2007).

1. The term "effective amount" should be construed to mean an amount of forskohlin that promotes lean body mass, where the effectiveness is systemic

The cited art did not disclose or suggest administering an "effective amount" of forskohlin to promote lean body mass. The Board adopted a construction of "effective amount" that was so broad that it is inconsistent with the specification and contrary to the established definition of this term, which this Federal Circuit recognizes as a standard term. *See Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1278 (Fed. Cir. 2003) *rev'd on other grounds*, 471 F.3d 1363 (Fed. Cir. 2006) (Because the patentee did not deviate from the accustomed meaning of the disputed claim term, the term "effective amount" is construed in view of its ordinary and customary meaning, i.e., "a sufficient amount of the specified component . . . having the specified properties under the specified conditions, if any.").

The Federal Circuit erroneously adopted the Board's position that the term "effective amount" should be construed to mean an amount of forskohlin that promotes lean body mass, where the effectiveness may be systemic ***or localized***. App., *infra*, A11. However, this claim construction ignores the disclosure that is repeated throughout Petitioner's specification, indicating that the purpose of maintaining or increasing lean body mass is to cause a reduction in body fat. Further, in the "Background of the Invention" section of the patent, Petitioner compared its invention to then-existing

products designed to decrease body fat. App., *infra*, A52-A53. Petitioner discloses that the effectiveness of the invention may be evaluated based on "ideal physiological proportions between lean and fat body mass" that are expressed using percentages, waist hip ratio ("WHR"), and/or body mass index ("BMI"). App., *infra*, A53, A57. These are all assessments of the ***systemic*** effectiveness of a weight loss program, not ***localized*** effectiveness. The patent specification eliminates the possibility that the term "effective amount" can be construed to include localized effectiveness that does not also result in systemic effectiveness.

The Federal Circuit has held that the prosecution record cannot enlarge the claims beyond what the inventor has presented as his invention. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1319 (Fed. Cir. 2005) (*en banc*) (rejecting a claim construction that was broader than the technical usage specific to the invention). The Federal Circuit departed from this fundamental principle in adopting the Board's construction of the term "effective amount."

The construction of the term "effective amount" adopted by the Board and affirmed by the Federal Circuit is not uniform with prior decision of the Federal Circuit in *Abbott v. Baxter* and *Phillips v. AWH Corp.*, and therefore Petitioner requests that this Court remand the '327 application to the PTO for further consideration consistent with these opinions.

2. The term "promoting" should be construed to mean increasing lean body mass, or, in the alternative, furthering lean body mass by increasing lean body mass or reducing body fat relative to lean body mass

The Federal Circuit also adopted the Board's construction of "promoting," which is so broad it is inconsistent with both the patent specification and the invention to which it gives legal effect. This construction is also contrary to the Federal Circuit's prior holdings. *See Phillips*, 415 F.3d at 1315 (claims "must be read in view of the specification, of which they are a part.") (citation omitted).

It should be noted that in *Phillips*, as in the present case, the overbreadth of the claim construction at issue was due to use of extrinsic evidence from a general dictionary definition, rather than the underlying definition contained in the patent specification. The Federal Circuit has limited the permissible level of reliance on extrinsic evidence in claim construction. *See Forest Labs., Inc. v. Abbott Labs.*, 239 F.3d 1305, 1311 (Fed. Cir. 2001) (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996)).

However, the Federal Circuit affirmed the Board's erroneous position that use of the term "promoting" in connection with "lean body mass" means increasing lean body mass, ***furthering lean body mass by maintaining lean body mass***, reducing body fat relative to lean body mass, ***inducing cAMP mechanisms, and improving***

absorption of nutrients and their preferential incorporation into lean body mass. App., *infra*, A10. This claim construction was based on the Board's use of a dictionary definition (App., *infra*, A100), and is at odds with the disclosure provided in Appellant's specification.

Petitioner has previously argued that the term "promoting" should be construed to mean "increasing" lean body mass, but the Federal Circuit declined to do so. The Federal Circuit also declined to modify the Board's construction to reflect that "promoting" refers to increasing lean body mass, and reducing body fat relative to lean body mass. The Board's construction (particularly "furthering lean body mass by maintaining lean body mass") encompasses maintaining lean body mass while gaining body fat. This is outside the scope of the invention, which "shifts the proportion between lean body mass and adipose tissue in favor of lean body mass in order to restore the ideal physiological proportions between lean and fat body mass." App., *infra*, A57. This shift may be measured using body fat percentages, waist hip ratio ("WHR"), and/or body mass index ("BMI"). App., *infra*, A53, A57.

The prosecution record cannot enlarge the claims beyond what the inventor has presented as his invention. *See Phillips*, 415 F.3d at 1319 (rejecting definitions broader than the technical usage specific to the invention). The Federal Circuit has departed from this fundamental principle in adopting the Board's construction of the term "promoting."

The Federal Circuit's affirmance of the Board's erroneous construction of the term "promoting" is in direct conflict with its decision in *Phillips v. AWH*, and Petitioner requests that this Court remand the '327 application to the PTO for further consideration in order to resolve this conflict.

C. There is No Support for the Federal Circuit's Adoption of the Board's Findings of Fact Regarding the Disclosures of Kazuo, Greenway III, and Greenway IV

The Federal Circuit affirmed incorrect findings of fact based on the Board's overly-broad and incorrect claim constructions of the terms "effective amount" and "promoting." The Federal Circuit therefore erroneously adopted the Board's holdings that the disclosure of Kazuo anticipates and/or obviates the claims, and that the disclosures of Greenway III and Greenway IV anticipate the claims. These findings of fact do not find any support in the record.

i. Kazuo does not inherently disclose administering an amount of forskohlin that increases lean body mass, or reduces body fat relative to lean body mass

Kazuo discloses that an extract from *Coleus forskohlii* root or powder may be used to promote lipid metabolism by activating AC, increasing cAMP levels, and activating a hormone-sensitive lipase. The extract was used to prevent fat from being stored in the body, thereby preventing obesity. The Board took the position that Kazuo inherently

promoted lean body mass and shifted the proportion of lean body mass and adipose tissue in favor of lean body mass. The Board concluded that these findings of fact established anticipation and/or obviousness. App., *infra*, A14. However, there was no disclosure of promoting lean body mass.

Preventing accumulation of excess body fat, as disclosed in Kazuo, does not shift the proportion of lean body mass and adipose tissue already present in the body of the human individual or promote lean body mass – instead, it merely *prevents* a shifting of the proportion of adipose tissue to lean body mass, which is not encompassed under any legally-correct construction of the presently-claimed invention. Kazuo only discloses that an unidentified extract of *Coleus forskohlii* prevents fat formation by causing AC activation.

Accordingly, Kazuo does not inherently anticipate or render obvious the claimed invention.

2. Greenway III and Greenway IV do not inherently disclose administering an amount of forskohlin that increases lean body mass, or reduces body fat relative to lean body mass

Greenway III and Greenway IV disclose a study in which obese subjects were topically administered a composition comprising forskohlin (25×10^{-5} mol/L) on one thigh, and a placebo was topically administered to the other thigh. The study duration was four weeks. All four women lost a mean of 1.0 +/- 0.61 cm more from the thigh treated with forskohlin cream than from the thigh treated

with placebo cream. Greenway III and Greenway IV concluded that ***local fat*** can be reduced by topical application of forskohlin cream, and that thigh girth loss with topical forskohlin cream does not require weight loss, and without weight loss, fat redistribution from thighs to intra-abdominal area seems unlikely. Greenway III and Greenway IV opined that the amount of fat mobilized would presumably redistribute through all other fat deposits. The Board took the position that Greenway III and Greenway IV inherently promote lean body mass in an individual in need thereof by topical administration of forskohlin in a lean body mass promoting effective amount to the thighs of obese women. The Board concluded that these findings of fact established anticipation. App., *infra*, A20.

Petitioner argued that regional lipolysis leads to systemic redistribution of body fat without affecting total body fat or systematically shifting the proportion of lean body mass and adipose tissue in favor of lean body mass, but the Board did not adopt this argument because it was allegedly too narrow an interpretation and required limiting claims to systemic use and effectiveness. App., *infra*, A20. However, Petitioner submits that the claims are in fact limited to systemic use and effectiveness for at least the reasons set forth above.

Accordingly, Greenway III and Greenway IV do not inherently anticipate the claimed invention.

D. The Federal Circuit Erred as a Matter of Law by Affirming the Board's Conclusions of Anticipation and Obviousness Based on Findings of Law and Fact not Supported by Substantial Evidence

Petitioner submits that because the Board's constructions of the terms "effective amount" and "promoting" were legally incorrect, and the Board's resulting factual findings regarding the disclosures of Kazuo, Greenway III, and Greenway IV were not supported by substantial evidence, the Board's legal conclusions of anticipation and obviousness were in error. The Federal Circuit's affirmance of these incorrect claim constructions and findings of anticipation and obviousness is also in error, and should be reversed. *See In re Zurko*, 258 F.3d at 1386.

E. The Federal Circuit Erred as a Matter of Law by Affirming the Board's Denial of Petitioner's Request for Remand for Further Proceedings

By adopting a new, legally-incorrect claim construction for the term "promoting," the Board effectively issued new rejections. The Federal Circuit failed to order the Board to reopen prosecution so that Petitioner could have a full and fair opportunity to respond to the new rejections. *See* 37 C.F.R. § 41.50(d).

Justice requires that Petitioner be given the opportunity to respond to this new interpretation of the claims, including amending the claims in a manner consistent with the new claim interpretation

adopted by the Board if it is valid. This can only be accomplished by reopening prosecution.

1. Standard of Review

A reviewing court must give deference to an agency's interpretation of its own regulations. *In re McDaniel,* 293 F.3d 1379, 1382 (Fed. Cir. 2002); *see also Martin v. Occupational Safety & Health Review Comm'n,* 499 U.S. 144, 150-51 (1991) ("[T]he reviewing court should give effect to the agency's interpretation so long as it is 'reasonable.'"). "However, such deference is not appropriate where the agency's interpretation is 'plainly erroneous or inconsistent with the regulation.'" *In re McDaniel,* 293 F.3d at 1385 (Fed. Cir. 2002) (citing *Auer v. Robbins,* 519 U.S. 452, 461 (1997)) (vacating Board's decision where its interpretation of 37 C.F.R. § 1.192 was "both plainly erroneous and inconsistent with the regulation.").

a. A Rejection Based On a New Claim Interpretation May Be Considered a New Ground of Rejection

If the Board issues a new rejection or maintains an existing rejection based on a new interpretation of the claims, this may constitute a new ground of rejection. In such a situation, the Board is required to follow 37 C.F.R. § 41.50(b), which allows Petitioner to reopen prosecution with the examiner.

In *Ex parte Felder*, No. APL 2008-3387, 2008 WL 3991998 (Bd. Pat. App. & Interf. Aug. 27, 2008), the Board maintained a rejection under 35 U.S.C. § 102(b) over a prior-art reference the examiner relied

on, but considered it a new ground of rejection because it was issued under a different claim interpretation. *Felder* involved, *inter alia*, an examiner's rejection of independent claim 26 under 35 U.S.C. § 102(b) in view of a German patent to Frener. In making his rejection, the examiner argued that claim 26 was of a certain scope. The Board interpreted claim 26 differently than the examiner. In adopting this new claim construction, the Board reversed the examiner's rejection of claim 26 as anticipated by Frener. However, the Board noted, "[n]onetheless the Examiner's identification of Frener as an anticipatory reference with regard to claim 26 was not wrong." (*Id.* at page 16.). The Board found the claim to be anticipated by Frener, and the Board issued another rejection of the same claim, also under 35 U.S.C. § 102(b). The Board held that "[b]ecause the proper construction of these claims differs from the one proposed by the Examiner, we enter this rejection as a NEW GROUND OF REJECTION . . . in order to provide Felder with a full and fair opportunity to respond." *Id.* at 18.

Thus, any rejection based on a new claim interpretation constitutes a new ground of rejection, and an appellant must be afforded the opportunity to respond to the new ground of rejection.[4]

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[4] *See also Ex parte Pennetreau*, No. APL 2000-0782, 2002 WL 33936334, at *3 (Bd. Pat. App. & Interf. Feb. 19, 2002) ("Since our claim construction, reasoning and analysis of the prior art differs from that presented by the examiner, we denominate this 'affirmance' of the examiner's rejection as a new ground of rejection under 37 C.F.R. § 1.196(b)."); *Ex parte Zasloff*, No. APL 2007-0055, 2007 WL 988644, at *7 (Bd. Pat. App. & Interf.

Petitioner submits that, similar to the proceedings of *Ex Parte Felder*, the Board adopted a new interpretation of claim 1 in the Decision on Appeal. Because Petitioner never had an opportunity to respond to the Board's new interpretation of claim 1, prosecution should be reopened to give Petitioner a full and fair opportunity to respond to the new ground of rejection, and to amend the claims in a manner consistent with the new interpretation adopted by the Board.

Moreover, the Board's new claim interpretation constitutes a new ground of rejection under the Federal Circuit's "basic thrusts" criterion for determining whether a rejection is new. *In re Kronig*, 539 F.2d 1300, 1302, 1303 (C.C.P.A. 1976); *see also In re Kumar*, 418 F.3d 1361, 1368 (Fed. Cir. 2005). If the "basic thrusts" of the Board's rejection and the examiner's rejection are not the same, "then the applicants would not already have had a 'fair opportunity' to respond to the thrust of the board's rejection before the examiner, and the board's rejection can fairly be said to warrant a further

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Jan. 24, 2007) ("This claim construction differs from the construction given to the claims by the Examiner . . . . For this reason, we designate our rejection, which is described in more detail below, as a new ground of rejection."); *Ex parte Laferriere*, No. APL 2007-3481, 2008 WL 2699983, at *9 (Bd. Pat. App. & Interf. July 8, 2008) ("We have taken administrative notice of certain facts . . . necessary to properly construe the limitation regarding operating system independence and interpret how Stein meets this limitation. Accordingly, we denominate this rejection of claim 16 under 35 U.S.C. § 103(a) as unpatentable over Stein and Ross as a new ground of rejection.").

opportunity for response." *In re Ansel*, 852 F.2d 1294, No. 88-1093, 1988 WL 63291, at *2 (Fed. Cir. June 23, 1988) (citing *In re Kronig*, 539 F.2d at 1302). Here, the Board's use of an extrinsic dictionary definition for "promote," not relied upon by the examiner, resulted in a new, broader claim interpretation. This manifestly presents a different "thrust of rejection" from the examiner's rejection. *See Application of Boon*, 439 F.2d 724, 727-28 (C.C.P.A. 1971) ("[C]itation by the board of a new reference, such as the dictionary in this case, and reliance thereon to support a rejection, will be considered as tantamount to the assertion of a new ground of rejection.").[5] The Board's rejection based on this noticeably-broader claim interpretation warrants a further opportunity for Petitioner to respond to the Board's rejection because Petitioner has not enjoyed a 'fair opportunity' to respond to the thrust of the Board's rejection before the examiner.

Petitioner respectfully requests that this Court remand the '327 application to the PTO under 37 C.F.R. § 41.50 for further proceedings.

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[5] Although the Court in *In re Boon* ultimately upheld the Board's findings, it did so because the judicially-noticed dictionary reference played only a "minor role" in filling in evidentiary gaps in the examiner's record. *Id.*, 439 F.2d at 727-28. The Board's use of the dictionary in this case, however, constituted an entirely new claim interpretation. This new claim interpretation did not play a "minor role" in the Board's affirmation of the examiner's rejection, but rather was a new ground of rejection constructed by the Board.

III. THIS CASE IS A GOOD VEHICLE FOR RESOLVING THE QUESTIONS PRESENTED

This case presents an opportunity for the Court to reiterate that patent holders have the right to a full and fair hearing before they can be deprived of their intellectual property rights, particularly in the context of patent-reexamination proceedings.

Because the Federal Circuit has exclusive jurisdiction over patent cases, there can be no split in the circuits on this issue. The opinions referenced herein have explored the issues raised in this case, and there is no need to wait for further development of the law. The inconsistent opinions of the Federal Circuit regarding issues of claim construction, and the treatment of new rejections that result from changes in claim interpretation on appeal, show that there has been a departure from the accepted and usual course of judicial proceedings. What is needed now is guidance from this Court.

Relatively few reexamination applications are filed as compared to the number of patents issued, and the reexamination applications in which new rejections are issued by the Board in the course of issuing decisions on appeal are even rarer. It is therefore unlikely that a better case addressing this issue will be presented any time soon.

IV. CONCLUSION

For the foregoing reasons, the petition for a writ of certiorari should be granted.

Respectfully Submitted,

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NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

2008-1257, 2009-1317
(Reexamination No. 90/007,327)

IN RE SAMI CHEMICALS AND EXTRACTS, LTD.

Judgment

ON APPEAL from the United States Patent and Trademark Office Board of Patent Appeals and Interferences.

in CASE NO(S). 90/007,237

This CAUSE having been heard and considered, it is

ORDERED and ADJUDGED:

Per Curiam (NEWMAN, LOURIE, and GAJARSA, Circuit Judges).

AFFIRMED. See Fed. Cir. R. 36.

ENTERED BY ORDER OF THE COURT

DATED FEB 19 2010 Jan Horbaly, Clerk

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SAMI CHEMICALS AND EXTRACTS, LTD,
Appellant

Appeal 2007-3482
Reexamination Control 90/007,327[1]
Patent 5,804,596
Technology Center 3900

Decided: December 13, 2007

Before TEDDY S. GRON, ADRIENE LEPIANE HANLON and CAROL A. SPIEGEL, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

DECISION ON APPEAL

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[1] The patent under reexamination is based on Application 08/807,652, filed 27 February 1997. The real parties in interest are said to be Sabinsa Corporation and Sami Labs Limited (Brief on Appeal filed 27 June 2006 ("App. Br.") at 1).

INTRODUCTION

Sami Chemicals and Extracts, Ltd. ("Appellant") appeals under 35 U.S.C. §§ 134 and 306 from the final rejections of claims 1-34. We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM.

THE SUBJECT MATTER ON APPEAL

The subject matter on appeal is directed to methods of promoting lean body mass "in a human individual in need thereof" by administering "an effective amount" of forskohlin, a compound isolated from *Coleus forskohli* plants, to the individual. Claims 1, 5, and 31 are illustrative of the subject matter on appeal and read as follows:

> 1. A method of promoting lean body mass in a human individual in need thereof, comprising administering to the individual a lean body mass promoting effective amount of forskohlin.
>
> 5. A method of shifting the proportion between lean body mass and adipose tissue in favor of lean body mass in a human individual in need thereof, comprising administering to the individual a proportion shifting effective amount of forskohlin.
>
> 31. The method of claim 1, wherein the method promotes the synthesis and secretion of hormones which promote lean body mass.

THE REJECTIONS

The Examiner relies upon the following references of record as evidence of unpatentability:

Kazuo[2] JP-6-133731 May 17, 1994

Greenway et al. ("Greenway III"), "Regional Fat Loss from the Thigh in Obese Women after Adrenegic Modulation," *Clinical. Therapeutics*, Vol. 9, No. 6, pp. 663-669 (1987).

Greenway et al. ("Greenway IV"), "Topical Fat Reduction," *Obesity Research*, Vol. 3, Suppl. 4, pp. 561S-568S (November 1995).

Appealed claims 1, 5, 9-10, and 31-34 stand rejected under 35 U.S.C. § 102(b) as anticipated by Kazuo; claims 1, 5, 1.1-12, and 31-34 stand rejected under 35 U.S.C. § 102(b) as anticipated by Greenway III or Greenway IV; claims 1-34 stand rejected under 35 U.S.C. § 103(a) over Kazuo; and, claims 31-32 stand rejected under 35 U.S.C. § 112, first paragraph (lack of written descriptive support) (Ans.[3] at 4, 5, 7, 8 and 11).

We have also considered the certified translation of Figure I of Kazuo, the Badmaev Declaration,[4] and the Godard[5] article provided by Appellant in support of its position (App. Br. at 34).

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[2] This decision refers and cites to the USPTO translation of Kazuo, "Diet Food," by Akiko Smith dated 25 August 2005 and to the certified English translation of Kazuo Diagram I supplied by the Appellant.

[3] Examiner's Answer mailed 7 November 2006 ("Ans.").

[4] Declaration under 37 C.F.R. § 1.132 by Dr. Vladimir Badmaev filed 23 February 2006 ("the Badmaev Declaration"). Dr. Badmaev is a named co-inventor of the patent under reexamination.

[5] Godard et al. ("Godard"), "Body Composition and Hormonal Adaptations Associated with Forskolin Consumption in Overweight and Obese Men," *Obesity Research*, Vol. 13, No. 8, pp. 1335-1343 (8 August 2005).

We have not considered the printout from the National Library of Medicine referenced in Appellant's Reply Brief since no printout was found attached thereto (Reply Br.[6] at 7).

Appellant has grouped the claims into three groups, i.e., (i) claims 1-4, 9, 11, 13, 15-17, 19, 21, 23, 25, 27, 29, and 33; (ii) claims 5-8, 10, 12, 14, 18, 20, 22, 24, 26, 28, 30, and 34; and, (iii) claims 31 and 32 (App. Br. at 3).

However, Appellant has not separately argued the patentability of claims 31 and 32 over the prior art (see e.g., App. Br. at 7 and 17). Therefore, we decided this appeal on the basis of claims 1 and 5 relative to the prior art; and, on the basis of claim 31 relative to written description. Further, arguments not raised in the principal brief are waived. 37 C.F.R. § 41.37(c)(1)(vii).

We preface our discussion of the rejection under § 112, first paragraph, by considering the disclosure of Appellant's specification; and, of the prior art rejections by construing the appealed claims.

FINDINGS OF FACT ("FF")

The following findings of fact are supported by a preponderance of the evidence of record.

A. The '596 patent specification

[1] The '596 specification describes "a method of promoting lean body mass in an individual,

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[6] Reply Brief under 37 C.F.R. § 41.41 filed 5 January 2007 ("Reply Br.").

comprising administering to the individual a lean body mass promoting effective amount of forskohlin" ('596 patent at 2:66 to 3:2).

[2] Forskohlin is said to be a chemical found in the *Coleus forskohli* plant that activates the enzyme adenylate cyclase (AC) ('596 patent at 3:12-13 and 46-47).

[3] Adenylate cyclase activation is said to initiate a cascade of processes, i.e., increased cyclic adenosine monophosphate (cAMP) levels, leading to activation of a hormone-sensitive lipase which releases fatty acids from body adipose depots, ultimately resulting in activation of triiodothyronine (T_3), activation of phosphorylase in skeletal muscles, insulin secretion and the synthesis and secretion of anabolic steroid hormones ('596 patent at 3:61 to 4:10).

[4] Stimulation with forskohlin is said to be known in the literature to result in a number of effects, including lipolysis in fat cells in vitro, potentiation of insulin secretion, increased synthesis of body steroids, increased release of adrenocorticotropic hormone (ACTH), and decreased intraocular pressure ('596 patent at 2:19-34).

[5] The '596 patent describes oral, topical or parenteral administration of forskohlin in an amount of from ~ 10 to ~ 60 mg/day to promote lean body mass ('596 patent at 4:23-25 and 47-48).

Other findings of fact follow below.

WRITTEN DESCRIPTION

The test for compliance with the written description requirement is whether the disclosure of the application, as originally filed, reasonably conveys to those skilled in the art that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

Claims 31 and 32 stand rejected under § 112 for insufficient written description. Representative claim 31 limits the method of claim I to a method which "promotes the synthesis and secretion of hormones which produce lean body mass." According to the Examiner, disclosure of "'the synthesis and secretion of *anabolic steroid* hormones' [in Appellant's specification] (column 4, lines 9-10), . . . does not provide full description of the genus, the hormones" (Ans. at 11, original emphasis, bracketed text added). The Examiner states that the term "hormones" includes both catabolic and anabolic hormones as well as steroid and non-steroid hormones (Ans. at 27). However, the Examiner has not provided any reasoned basis for her interpretation of claim 31. To the contrary, the 596 patent discloses that stimulation with forskohlin is said to be known in the literature to result in increased synthesis of body steroids and increased secretion of ACTH, a peptide hormone (FF 4). The Examiner has not explained why one skilled in the art would not have found these disclosures reasonably sufficient to provide written support for the method of claim 31. Indeed, in *In re Herschler*,

591 F.2d 693, 697 (CCPA 1979), the court found adequate written descriptive support for broad claims to processes for topically administering a physiologically active steroidal agent to a human or animal by concurrently administering the steroidal agent with dimethyl sulfoxide ("DMSO"), even though the specification only disclosed one example of a "physiologically active steroidal agent." As the court noted, "[w]ere this application drawn to novel 'steroidal agents,' a different question would be posed." *Id.* at 701.

Since the Examiner has failed to establish that the '596 specification would not have reasonably conveyed the method of claim 31 to one skilled in the art, we REVERSE the rejection of claims 31 and 32 under § 112, first paragraph.

ANTICIPATION AND OBVIOUSNESS

The scope and content of claimed subject matter must first be determined in order to explore the relationship of the invention claimed to the prior art. *In re Steele*, 305 F.2d 859, 862 (CCPA 1962). Accordingly, we first determine the scope and content of the claimed subject matter. In particular, we address the meaning of the terms "promoting," "administering," an "effective amount," and "a human individual in need thereof' as recited in the claims on appeal.

A. Claim construction

Claims in reexamination "will be given their broadest reasonable interpretation." *In re Yamamoto*, 740 F.2d 1569, 1571 (Fed. Cir. 1984). *See In re Zletz*, 893 F.2d 319, 322 (Fed. Cir. 1989) ("An essential purpose of patent examination is to fashion

claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainities of claim scope be removed, as much as possible, during the administrative process.").

1. "promoting"

The ordinary meaning of "promoting" is, in relevant part, to further or help bring into being (see e.g., Merriam-Webster's COLLEGIATE DICTIONARY, tenth edition (1998) at 933 (copy attached)). The language, "A method of promoting lean body mass," of claim 1 is unambiguous on its face. Moreover, construing "promoting" as furthering or helping to bring about is consistent with the '596 specification.

[6] According to Appellant's specification, forskohlin is believed to promote formation of lean body mass by improving absorption of nutrients and their preferential incorporation into lean body mass via activation of AC and the resulting increased levels of cAMP and its actions ('596 specification at 3:45-53).

[7] Further according to the '596 specification, the prior art suggests that the known in vitro lipolysis (hydrolytic degradation of fat) effect of forskohlin in adipocytes (fat cells) is due to increased levels of cAMP and its actions ('596 specification at 2:19-26).

[8] More generally, the '596 specification states that "an ideal weight management approach should be to reduce body weight to acceptable levels by restoring the optimal proportions of fat to lean body mass" ('596 specification at 1:67 through 2:3).

[9] In other words, "the general purpose of improving the overall health" of an individual would be served "[b]y maintaining or increasing the lean body mass while simultaneously reducing body fat" ('596 specification at 2:3-6).

Therefore, we broadly interpret "promoting" lean body mass, consistent with the '596 specification, as "furthering or bringing about" lean body mass. "Promoting" lean body mass is not limited solely to "increasing" lean body mass, but also encompasses furthering lean body mass by maintaining lean body mass; reducing body fat relative to lean body mass; inducing cAMP mechanisms; and, improving absorption of nutrients and their preferential incorporation into lean body mass.

2. "administering"

There are a number of conventional, well-known ways of administering a compound or composition. Among the most common are oral ingestion; intravenous, subcutaneous or intramuscular parental injection; and, topical administration to the skin or mucous membranes. The '596 specification describes oral, topical and parental administration of forskohlin (FF 5). Appellant individually claims oral (claims 9-10, 17-18, 21-22, 25-26, and 29-30), topical (claims 11 and 12), and parenteral (claims 12 and 14) administration of forskohlin. Therefore, we broadly construe "administering," as recited in both independent claims 1 and 5 as encompassing any

conventional, well known way of administering a compound or composition.

3. "effective amount"

Claims 1 and 5 recite administering "a lean body mass promoting effective amount" and "a proportion shifting effective amount" of forskohlin, respectively. We broadly construe the "effective amount" of forskohlin recited in claim I as an amount which promotes lean body mass. We broadly construe the "effective amount" of forskohlin recited in claim 5 as an amount which shifts the ratio of lean body mass to fat in favor of lean body mass by either reducing the amount of fat while simultaneously maintaining or increasing lean body mass or by increasing the amount of lean body mass while simultaneously maintaining or decreasing fat.

We further construe the scope of an "effective amount" broadly to encompass both systemic and localized effectiveness. The '596 specification provides for the same amount of forskohlin, i.e., ~10 to ~ 60 mg/day, to be administered orally, topically or parenterally (FF 5). The '596 specification is silent as to minimum blood levels or other systemic indicators of forskohlin concentration needed for effectiveness to promote lean body mass or to shift the ratio of lean body mass to fat in favor of lean body mass.

4. "human individual in need thereof"

The claims require that the method be performed on "a human individual in need thereof' and that the method be used for "promoting lean body mass" (claim 1) or for "shifting the proportion between lean body mass and adipose tissue in favor

of lean body mass" (claim 5). The claimed invention is not limited to treating obesity or weight excess and, therefore, is not limited to an obese or an overweight individual. The '596 specification does not specifically define a "human individual in need" of the claimed method. Therefore, we broadly construe a "human individual in need thereof' to be an individual wanting more lean body mass or wanting to lessen or prevent accumulation of fat (adipose tissue). In other words, a "human individual in need thereof," as recited in the appealed claims, encompasses an obese person wanting to decrease body fat, a person seeking to prevent accumulation of excess body fat, and a weightlifter wanting to increase muscle mass.[7]

B. Anticipation

Claimed subject matter is anticipated if "each and every limitation is found either expressly or inherently in a single prior art reference." *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1374 (Fed. Cir. 2001). The doctrine of inherency may not be used to establish anticipation unless a prior inherency can be established as a

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[7] See e.g., The transcript of the oral hearing at 7:22 through 8:3, i.e.,

MR. BERMAN: In other words, the weightlifter example you gave I think is a suitable example where the weightlifter may be in an ideal physical condition, but yet still may wish to promote even more lean body mass by taking this nutritional supplement.

JUDGE SPIEGEL: So given this discussion, am Ito understand that a human individual in need thereof is a subjective determination?

MR. BERMAN: Yes, I believe that's the position that the federal circuit is taking as well.

certainty. Probabilities or possibilities will not be sufficient to establish an inherent event. *Continental Can Co. U.S.A., Inc. v. Monsanto, Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991).

1. Anticipation based on Kazuo

Claims 1, 5, 9-10, and 31-34 stand rejected under 35 U.S.C. § 102(b) as anticipated by Kazuo (Ans. at 4-5).

[10] Kazuo discloses a diet food containing a plant extract from *Coleus .forskohlii* root or powder which "selectively promotes a lipid metabolism" by activating AC, thereby increasing cAMP levels, which leads to activation of a hormone-sensitive lipase (Kazuo at 3, ¶ 5).

[11] According to Kazuo, "[t]he present invention attempts to present an effective diet food that can prevent fat from being stored in a body while eating freely to take the necessary nutrients" (Kazuo at 2, ¶ 3).

[12] In Experiment II, seven female volunteers took a forskohlin plant extract supplement three times a day before eating a normal meal for two weeks (Kazuo at 7, ¶ 10).

[13] Experiment II was said to recognize the effectiveness of forskohlin extract "for prevention of obesity" (Kazuo at 8, ¶ 11).

[14] Kazuo concluded that by taking forskohlin as a dietary supplement "one can prevent the fat accumulation in one's body while eating normally and taking necessary nutrition" (Kazuo at 8, ¶ 12).

[15] The Examiner finds that Kazuo's method inherently promotes lean body mass and a shift in the proportion of lean body mass and adipose tissue in favor of lean body mass as recited in claims 1 and 5, respectively (Ans. at 4-5).

The Examiner's findings are sufficient to establish a prima facie case of anticipation. Experiment II of Kazuo is directed to prevention of obesity (FF 13), i.e., preventing accumulation of excess body fat (see e.g., Merriam-Webster's COLLEGIATE DICTIONARY, tenth edition (1998) at 801 (copy attached)). Preventing accumulation of excess body fat shifts the proportion of lean body mass and adipose tissue in favor of lean body mass as recited in claim 5 and promotes lean body mass as recited in claim 1. Moreover, Kazuo recognizes that forskohlin stimulates AC-activation induced increases of cAMP mechanisms (FF 10), which also promotes lean body mass as recited in claim 1. The volunteers participating in Experiment II were administered an amount of forskohlin effective for the prevention of obesity and are "humans in need thereof" by virtue of wanting to prevent fat accumulation (FFs 13 and 14).

Appellant argues that Kazuo does not administer "an effective amount" of forskohlin (App. Br. at 8-12 and 17-18) to "a human in need thereof," as required by claims 1 and 5 (App. Br. at 13-18).

According to Appellant, "Kazuo et al. is intended to address fat reduction and accumulation of fat" whereas "the present invention can even be achieved without weight loss" as evidenced by the

Godard paper (App. Br. at 16, original emphasis). Appellant argues that Table 1 of Godard shows that those receiving forskohlin maintained the same overall body weight, while increasing lean body mass and decreasing fat mass (App. Br. at 16). Thus, Appellant concludes that the female volunteers in Kazuo are not "humans in need thereof" as recited in the appealed claims (App. Br. at 16).

[16] Table 1 in Godard is said to show a significant difference between changes in fat mass and bone mass in forskohlin- and placebo-treated subjects, but not in changes in body weight or lean body mass (Godard at 1337, Table 1, column titled "Change (pre - post)").

[17] Notably, a significant increase in lean body mass is said to be shown in both forskohlin- and placebo-treated subjects on an individual basis (Godard at 1337, Table 1, lines 6 and 11 (each beginning with "LBM (kg)")).

A person, such as a female volunteer in Kazuo's Experiment II, who wants to prevent excess fat accumulation (having too much adipose tissue) is a "human in need" of promoting lean body mass and/or shifting the proportion of lean body mass/adipose tissue in favor of lean body mass giving the claim term its broadest reasonable interpretation consistent with Appellant's specification (see claim construction § A.4). As discussed above, the claimed invention is not limited to treating a human with obesity or pure weight excess issues. Similarly, as pointed out by the Examiner (Ans. at 20), the claimed invention does not require that lean body mass promotion and/or shifting the proportion of

lean body mass and adipose tissue in favor of lean body mass be achieved without weight loss. Finally, Godard is of little, if any, probative value. Appellant has not explained the tests, data or significance of the results described in Godard in general, or listed in Table 1 in particular (App. Br. at 16). For example, according to Table I in Godard, a significant increase in lean body mass is said to have been shown in the test subjects, whether they received forskohlin or not (placebo) (FF 17). In short, Appellant has failed to show that the Examiner erred in finding that the human volunteers of Kazuo are "human[s] in need thereof as recited in claims 1 and 5 (Ans. at 19). *See e.g., Mehl/Biophile International Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) (finding anticipation of a method of hair depilation by an article teaching a method of skin treatment but recognizing the disruption of hair follicles, citing In re King, 801 F.2d 1324, 1326 (Fed. Cir. 1986)).

Appellant also argues that Kazuo does not disclose or suggest administering "an effective amount" of forskohlin as claimed, relying on the Badmaev Declaration to support its position.

[18] Vladimir Badmaev is a co-inventor of the '596 patent and Vice President of Medical and Scientific Affairs of Sabinsa Corporation, one of the assignees of the '596 patent (Badmaev Declaration at 1, ¶ 1).

[19] Dr. Badmaev testified that data from two clinical studies showed that "in subjects provided with an oral dose of 50 mg forskohlin per day, at least 3 months of treatment is

needed for a significant loss in body weight, and at least 8 weeks of treatment is needed to significantly increase lean body mass" (Badmaev Declaration at 2, ¶ 3).

Appellant calculated that Kazuo administered a daily dose of about 3.186 mg forskohlin per day to each subject during the two week duration of Experiment II (App. Br. at 9). According to Appellant, this is too small a dosage over too short a time period to change body composition in any meaningful way and, therefore, Kazuo does not disclose or suggest an "effective amount" of forskohlin as required by the claimed invention (App. Br. at 9).

Even assuming *arguendo* that each subject ingested ~3.1.86 mg forskohlin per day in Kazuo's Experiment II, this argument is not persuasive of Examiner error. None of the claims on appeal require any minimum degree or amount of lean body mass promotion or shift in the proportion of lean body mass/adipose tissue in favor of lean body mass, let alone some undefined "significant increase" in lean body mass. For example, claim 5 is directed to a method of shifting the proportion of lean body mass/adipose tissue in favor of lean body mass. Decreasing the amount of adipose tissue without affecting lean body mass (e.g., fat reduction as addressed by Kazuo) would shift their relative proportion as required by claim 5. Furthermore, lean body mass may be "promoted" by various means including reducing body fat relative to lean body mass and inducing cAMP mechanisms (which Kazuo recognizes forskohlin does). Moreover, whether the subjects in Kazuo's Experiment II experienced any

"significant" loss in body weight is irrelevant to the claimed invention which is not directed to a method of "significant" weight loss. Finally, the Badmaev Declaration is of little, if any value, in rebutting the Examiner's prima facie case of anticipation because it fails to set forth a nexus between the claimed invention and the supporting evidence. The claimed invention is not limited to oral administration of 50 mg per day of forskohlin in an extract of unknown composition for at least 8 weeks to obese and/or overweight subjects. The Badmaev Declaration is silent as to other possible contributory factors to weight loss and/or increased lean body mass, e.g., increased exercise or walking, decreased total caloric intake, increased water intake, etc. *In re Grunwell*, 609 F.2d 486 (CCPA 1979); *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). In other words, the Badmaev Declaration failed to establish a nexus between the claimed invention and the data from the two clinical studies relied upon. Thus, Appellant has failed to show that the Examiner erred in finding that Kazuo administered "an effective amount" of forskohlin to the volunteers of Experiment II.

Based on the foregoing, we AFFIRM the rejection of claims 1, 5, 9-10, and 31-34 under § 102(b) as anticipated by Kazuo.

2. Anticipation based on Greenway III or IV

Claims 1, 5, 11-12, and 31-34 stand rejected under 35 U.S.C. § 102(b) as anticipated by Greenway III or Greenway IV[8] (Ans. at 5-8).

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[8] As noted by Appellant (App. Br. at 18), the disclosures of Greenway III and Greenway IV appear to be cumulative.

[20] In the respective study 3s of Greenway III and IV, four obese women topically administered a forskohlin (colforsin) cream (25 x 10-5 mol/L) to one thigh and a placebo cream to the other for four weeks (Greenway III at 664 and 667; Greenway IV at 565S).

[21] All four women lost a mean of 1.0 ± 0.61 cm more girth from the thighs treated with forskohlin cream than from the control thighs (Greenway III at 667 and Figure 4; Greenway IV at 566S and Figure 4).

[22] Greenway III and IV concluded that local fat can be reduced with topical application of forskohlin cream (Greenway III at 669; Greenway IV at 567S).

[23] Greenway IV further concluded that thigh girth loss with topical forskohlin cream does not require weight loss; and, without weight loss, redistribution of the fat from the thighs to the intra-abdominal area seems unlikely (Greenway IV at 567S, col. 2, ¶ 3).

[24] Greenway IV goes on to state that "[t]he amount of fat mobilized Would presumably redistribute through all other fat depots" (Greenway IV at 567S, col. 2, ¶ 3).

[25] Greenway IV still further concluded that since many women, whether or not they are obese, are concerned about the appearance of their thighs and the women receiving this cream "experienced an improved self-image which can result in tangible improvements in their perceived quality of life" (Greenway IV at 567S, col. 2, ¶ 4).

[26] The Examiner finds that Greenway's (citing Figures 4 of Greenway III and IV) method inherently promotes lean body mass or shifts the proportion between lean body mass and adipose tissue in favor of lean body mass in an individual in need thereof by topical administration of forskohlin in a lean body mass promoting effective amount or proportion shifting amount to the thighs of obese women (Ans. at 6-8).

The Examiner's findings are sufficient to establish a prima facie case of anticipation. The respective study 3s of Greenway III and IV describe a method of localized fat (adipose tissue) reduction in a woman's thigh by topical administration of an effective amount of forskohlin cream to the thigh of a human individual in need thereof (FFs 20-22), i.e., a method of promoting lean body mass or proportion shifting the lean body mass/adipose tissue ratio in favor of lean body mass as recited in claims 1 and 5. Further, Greenway IV teaches that such a human individual in need thereof may or may not be an obese woman (FF 23).

Appellant argues that the regional (thigh) lipolysis of Greenway III/IV leads to a systemic redistribution of body fat, without affecting total, body fat or systemically shifting the proportion of lean body mass and adipose tissue in favor of lean body mass (App. Br. at 19). However, we decline to adopt Appellant's narrow interpretation limiting the claimed invention to systemic use and effectiveness (see claim construction discussion above).

Specifically, Appellant argues that Greenway III/IV fails to administer an "effective amount" of forskohlin (App. Br. at 20-22 and 24-25) to a "human individual in need thereof' (App. Br. at 23-25). Based on the Badmaev Declaration, and assuming that topical and oral dosing provide equivalent in vivo levels of forskohlin, Appellant calculates that "the subjects in Study 3 would have required about Y2 liter of ointment per application" and such levels would not have been used in the Greenway studies (App. Br. at 21). Acknowledging that forskohlin might have produced localized fat reduction in the Greenway studies, Appellant nevertheless argues that the fat mobilized from the thighs would presumably redistribute elsewhere (App. Br. at 22). Finally, Appellant argues that dosage regime of Greenway III/IV is insufficient to provide an effective amount of forskohlin in view of the Badmaev Declaration showing that an oral dose of 50 mg forskohlin per day significantly increased lean body mass only after eight weeks of treatment (App. Br. at 22).

As discussed above, we construe the scope of an "effective amount" broadly to encompass both systemic and localized effectiveness. Greenway III/IV disclose localized effective promotion of lean body mass and shifting of the ratio of lean body mass/adipose tissue in favor of lean body mass (FFs 20-22; see also Ans. at 22). None of the claims on appeal require any minimum degree or amount of lean body mass promotion or proportional shift in lean body mass/adipose tissue ratio, let alone an undefined "significant increase" in lean body mass. Secondly, Appellant has overstated Greenway IV's

position on fat redistribution. According to Greenway IV, redistribution of fat from the thighs to the infra-abdominal area seems unlikely in the absence of weight loss; and, thigh girth reduction does not require weight loss (FF 23). Nonetheless, redistribution of fat from one depot (e.g., thigh) to another depot (e.g., infra-abdominal area) is only an issue if the claims are limited to systemic effectiveness, which they are not. Finally, the Badmaev Declaration is entitled to little, if any, weight for the reasons discussed above in regard to the Kazuo-based anticipation rejection. Thus, for the reasons given, Appellant has failed to show that the Examiner erred in finding that Greenway III and IV each administered an "effective amount" of forskohlin as required by claims 1 and 5.

Appellant also argues that neither Greenway III nor IV administer forskohlin to "a human individual in need thereof' because regional lipolysis does not necessarily lead to total body fat or weight reduction (App. Br. at 23 and 25). A woman who wants to reduce the girth of her thighs by reducing the fat accumulated therein is a "human in need" of promoting lean body mass and/or shifting the proportion of lean body mass/adipose tissue in favor of lean body mass, albeit localized to her thighs, giving the claim term its broadest reasonable interpretation consistent with Appellant's specification. Since we decline to adopt Appellant's narrow construction of the claimed invention, we are not persuaded by this argument Hence, Appellant has failed to show that the Examiner erred in finding that the women participating in study 3 of Greenway III and Greenway IV are "human[s] in

need thereof' as recited in claims 1 and 5 (Ans. at 24).

Based on the foregoing, we AFFIRM the rejections of claims 1, 5, 11-12, and 31-34 under § 102(b) as anticipated by either Greenway III or Greenway IV.

C. Obviousness

A claimed invention is not patentable if the subject matter of the claimed invention would have been obvious to a person having ordinary skill in the art. 35 U.S.C. § 103(a); *KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727 (2007); *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966). Facts relevant to a determination of obviousness include (1) the scope and content of the prior art, (2) any differences between the claimed invention and the prior art, (3) the level of ordinary skill in the art, and (4) relevant objective evidence of obviousness or non-obviousness. *KSR*, 127 S.Ct. at 1734; *Graham*, 383 U.S. at 17-18. It is well settled that "anticipation is the epitome of obviousness." *Cornell v. Sears Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983) (quoting *In re Fracalossi*, 681 F.2d 792, 794 (CCPA 1982)).

Claims 1-34 stand rejected under 35 U.S.C. § 103(a) as obvious over Kazuo (Ans. at 8-11).

Appellant submits that claims 1-34 are unobvious over Kazuo for the same reasons claims 1, 5, 9-10, and 31-34 are not anticipated by Kazuo (App. Br. at 26-28). We find claims 1, 5, 9-10, and 31-34 to be anticipated by Kazuo under 35 U.S.C. § 102(b). Since "anticipation is the epitome of obviousness," we conclude that claims 1-34 are

rendered obvious under 35 U.S.C. § 103(a) over Kazuo. *Fracalossi*, 681 F.2d at 794.

Based on the foregoing, we AFFIRM the rejection of claims 1-34 under § 103(a) as obvious over Kazuo.

CONCLUSION

Upon consideration of the record and for the reasons given, it is

ORDERED that the Examiner's rejection of claims 31 and 32 as unpatentable under 35 U.S.C. § 112, first paragraph, is REVERSED;

FURTHER ORDERED that the Examiner's rejection of claims 1, 5, 9¬10, and 31-34 as unpatentable under 35 U.S.C. § 102(b) as anticipated by Kazuo is AFFIRMED;

FURTHER ORDERED that the Examiner's rejection of claims 1, 5, 11-12, and 31-34 as unpatentable under 35 U.S.C. § 102(b) as anticipated by either Greenway III or Greenway IV is AFFIRMED;

FURTHER ORDERED that the Examiner's rejection of claims 1-34 as unpatentable under 35 U.S.C. § 103(a) as obvious over Kazuo is AFFIRMED; and

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

MAT

Enc: USPTO translation of Kazuo by Akiko Smith dated 25 August 2005.

Merriam-Webster's COLLEGIATE DICTIONARY, tenth edition (1998) at 801 and 933.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte SAMI CHEMICALS AND EXTRACTS, LTD.,
Appellant

Appeal 2007-3482
Reexamination Control 90/007,327
Patent 5,804,596
Technology Center 3900

Decided: February 2, 2009

Before CAROL A. SPIEGEL, ROMULO H. DELMENDO, and ERIC GRIMES, *Administrative Patent Judges.*[1]

SPIEGEL, *Administrative Patent Judge.*

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[1] Administrative Patent Judges Teddy S. Gron and Adriene Lepiane Hanlon participated in our 13 December 2007 Decision but Judge Gron has retired and Judge Hanlon is unavailable. Accordingly, Administrative Patent Judges Eric Grimes and Romulo H. Delmendo have replaced them on this panel. *Cf. In re Bose Corp.*, 772 F.2d 866, 869 (Fed. Cir. 1985).

DECISION ON REHEARING

Appellant requests hearing under 37 C.F.R. § 41.52 of the Decision on Appeal mailed December 13, 2007 ("BPAI Decision"). Appellant argues that the Decision was based on a new claim interpretation not previously presented to Appellant during prosecution, thereby constituting a new ground of rejection (RR[2] 1). Appellant argues it is entitled to a full and fair opportunity to respond to the alleged new ground of rejection (RR 1-2). "To this end, Appellants respectfully request reopening of prosecution under 37 C.F.R. § 41.50(b)(1) and remand of the case to the Examiner, so that Appellants may amend the claims and otherwise respond to the outstanding rejections in a manner consistent with the new claim construction adopted by the Board" (RR 2). (Prosecution after a final decision of the Board can only be reopened under 37 C.F.R. § 41.50 in reexamination proceedings. See 37 C.F.R. §§ 1.114, 1.114(e)(5), and 1.198.) We conclude that our affirmance of the Examiner's rejections under 35 U.S.C. §§ 102(b) and 103(a) does not amount to a new ground of rejection.

Claims 1 and 5, the only independent claims on appeal, are illustrative of the subject matter on appeal and read (emphasis added):

> 1. A method of promoting lean body mass in a human individual in need thereof, comprising administering to the individual a

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[2] Request For Rehearing Under 37 C.F.R. § 41.52 filed 25 September 2008 ("RR").

lean body mass promoting effective amount of forskohlin.

5. A method of *shifting the proportion between lean body mass and adipose tissue in favor of lean body mass* in a human individual in need thereof, comprising administering to the individual a proportion shifting effective amount of forskohlin.

Findings of fact set forth in this Decision are supported by a preponderance of the evidence of record.

I. Procedural History

[1] U.S. Patent 5,804,596 ("the 596 patent") issued on September 8, 1998 with eight claims.

[2] A request for ex parte reexamination of the 596 patent was filed by the patent owner (Appellant) on December 1, 2004, and assigned reexamination control number 90/007,327.

[3] An Order granting reexamination of all of the claims of the 596 patent was mailed on February 4, 2005.

[4] The reexamination proceeding progressed to a point where, on December 23, 2005, an Office action was mailed, in which all of the claims then pending in the reexamination, claims 1-34, were finally rejected.

[5] An improper Request for Continued Examination (RCE) with an amendment, affidavit, drawings, and translation, was filed

on February 23, 2006. On March 9, 2006, Appellant was notified that the amendment was improper because it failed to comply with 37 C.F.R. § 1.530(d)-U). Another response was filed on March 20, 2006.

[6] In a decision mailed April 6, 2006, the improper RCE papers were returned to Appellant and the amendment was placed in the file for consideration by the Examiner as a response to the final rejection.

[7] The Examiner mailed an advisory action on April 21, 2006, stating that the response to the final rejection had been considered but did not overcome all of the rejections and that the amendment would be entered upon filing an appeal.

[8] The final rejection was appealed. An Appeal Brief was filed on June 27, 2006. An Examiner's Answer was mailed on November 7, 2006. A Reply Brief was filed on January 5, 2007.

[9] After an oral hearing on October 17, 2007, the BPAI Decision was mailed on December 13, 2007. In the BPAI Decision, the rejection of claims 31 and 32 under 35 U.S.C. § 112, first paragraph, was reversed, but the rejections of (a) claims 1, 5, 9, 10, and 31-34 under 35 U.S.C. § 102(b) as anticipated by Kazuo, (b) claims 1, 5, 11, 12, and 31-34 under 35 U.S.C. § 102(b) as anticipated by Greenway III or Greenway IV, and (c) claims 1-34 under 35 U.S.C. § 103(a) as obvious over Kazuo were sustained.

[10] On February 11, 2008, Appellant filed a petition under 37 C.F.R. § 1.182 requesting continued examination of the 596 patent, which included a supplemental amendment seeking to cancel claims 5-8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, and 34 and to replace the terms "promoting" or "promotes" in claims 1 and 31, respectively, with "increasing" or "increases." Concurrently, Appellant filed a notice of appeal to the U.S. Court of Appeals to the Federal Circuit for review of the Decision.

[11] On March 6, 2008, the Office of Patent Legal Administration granted the petition under 37 C.F.R. § 1.182.

[12] On March 28, 2008, the Office of Patent Legal Administration mailed a decision vacating its March 6, 2008 decision, stating it lacked jurisdiction and referring the matter to the Office of the Solicitor.

[13] On April 3, 2008, Appellant filed a motion requesting a limited remand from the Federal Circuit to the Office for the purpose of allowing the Office to decide Appellant's February 11, 2008 petition.

[14] On May 29, 2008, the Federal Circuit granted Appellant's motion for limited remand. The Federal Circuit's order stated that the "motion for a limited remand is granted for the purpose of allowing the Board to consider" Appellant's position.

[15] On June 9, 2008, Appellant and the USPTO jointly moved under Federal Circuit Rule 27(1) for reconsideration of the Court's May 29, 2008 order, requesting that the Court clarify its order to specify that the remand was to the USPTO rather than to the Board.

[16] On July 17, 2008, the Court issued an order granting the parties' motion for reconsideration and clarifying that the "case is remanded for the limited purpose of allowing the PTO to consider Sami Chemicals' petition."

[17] On July 28, 2008, the Office of the Solicitor denied Appellant's petition under 37 C.F.R. § 1.182 because prosecution can only be reopened after a final decision by the Board under 37 C.F.R. § 41.50 in reexamination proceedings. See 37 C.F.R. §§ 1.114, 114(c)(5), and 1.198. The Solicitor concluded Appellant had directed its petition to the wrong entity.

[18] Concurrently, the Board *sua sponte* ordered the applicable rules waived and gave Appellant sixty days from July 28, 2008 in which to file a request for rehearing under 37 C.F.R. § 41.52 of the BPAI Decision of December 13, 2007.

[19] Appellant timely filed its request for rehearing on 25 September 2008.

II. Request for Rehearing

[20] Appellant summarized its request for reconsideration as follows:

Appellants request rehearing under 37 C.F.R. § 4152 and submit that the Board issued a new ground of rejection in the Decision on Appeal. Appellants submit that the new ground of rejection is based on a new claim interpretation not previously presented to Appellants during prosecution. Appellants submit that they are entitled to a full and fair opportunity to respond to the new ground of rejection. To this end, Appellants respectfully request reopening of prosecution under 37 C.F.R. § 41.50(b)(1) and remand of the case to the Examiner, so that Appellants may amend the claims and otherwise respond to the outstanding rejections in a manner consistent with the new claim construction adopted by the Board. (RR 2.)

[21] Four claim terms were construed by the Board in the BPAI Decision ---"promoting," "administering," "effective amount," and "human individual in need thereof' (BPAI Decision 7-10).

[22] The Board found the ordinary meaning of "promoting" is to further or help bring into being and t'.at the language, "[a] method of promoting lean body mass," of claim 1 was unambiguous on its face (BPAI Decision 7).

[23] The Board

broadly interpret[ed] "promoting" lean body mass, consistent with the '596 specification, as "furthering or bringing about" lean body mass. "Promoting" lean body mass is not limited solely to "increasing" lean body mass, but also

encompasses furthering lean body mass by maintaining lean body mass; reducing body fat relative to lean body mass; inducing cAMP mechanisms; and, improving absorption of nutrients and their preferential incorporation into lean body mass. (BPAI Decision 8).

[24] Appellant contends that during prosecution "both the Appellants and the Examiner presumed the term 'promoting' in claim 1 meant 'increasing'" (RR 4).

[25] However, according to the Background of the Invention section of the '596 patent, prior art

> weight control means do not take into account the importance of maintaining or increasing the lean body mass in the process of weight loss. (Spec. 1:58-60).
>
> . . . By maintaining or increasing the lean body mass while simultaneously reducing body fat, the weight loss regimen would serve the general purpose of improving the overall health of the individual.
>
> Maintaining or increasing the lean body mass (for example, skeletal muscles) is one of the important considerations for any weight loss strategy because lean body mass determines the rate of metabolism and the body's thermogenic response to food, and food induced thermogenesis and the metabolic rate, in turn, control body weight by an increased metabolism of body fat. (Spec. 2:3-13).

[26] The '596 patent describes the invention as

> . . . shift[ing] the proportion between lean body mass and adipose tissue in favor of lean body mass in order to restore the ideal physiological proportions between lean and fat body mass . . . (Spec. 3:37-41).
>
> . . . the present inventors believe that the invention increases the lean body mass by stimulating the enzyme adenylate cyclase (AC), with a resulting increase in the levels of cAMP. The increase[d] levels of cAMP in the tissues correspond well to enhancing the thermogenic response to food. An increase in the thermogenic response to food, in turn, improves absorption of nutrients and their preferential incorporation into lean body mass. Thus, the formation of lean body mass is promoted. (Spec. 3:45-53)

[27] According to Appellant, "[b]y focusing on the maintenance of lean body mass during dieting, the present inventors have made a significant advance in approaches to weight management" (App. Br.[3] 4).

[28] Further according to Appellant, prior art "weight control programs do not take into account the importance of maintaining or increasing lean body mass in the process of weight loss. . . By maintaining or increasing the lean body mass while reducing body fat, the present invention serves the general purpose of improving the overall health of the individual" (App. Br. 4).

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[3] Brief on Appeal filed 27 June 2006 ("App. Br.").

[29] Appellant argues that "[t]he distinctions of a 'lean body mass promoting effective amount' or a 'proportion shifting effective amount' of forskohlin, and the administration to a 'human individual in need thereof . . . distinguish the invention not only from the art cited in the initial prosecution of the '596 patent, but also from the art currently cited by the Examiner" (App. Br. 5-6).

[30] Appellant presented essentially the same patentability arguments against claims 1 and 5 (App. Br. 17, 24, and 27).

[31] The Examiner found, in part, that claims 1 and 5 are anticipated under 35 U.S.C. § 102(b) over the same references, i.e., Kazuo, Greenway III, or Greenway IV (Ans.[4] 4-8).

[32] For example, the Examiner stated "[t]he Greenway references have clearly shown that the forskohlin-treated thigh loses more girth than the control thigh . . . Lean body mass has the ordinary meaning of the mass of the body minus fat. Accordingly, reduction of thigh girth, which is indicative of localized fat reduction, would translate to promotion of localized lean body mass" (Ans. 22).

[33] Appellant does not dispute the reasonableness of the Board's claim construction or dispute its holding that (i) claims 1, 5, 9, 10, and 31-34 are unpatentable under § 102(b) as anticipated by Kazuo, (ii) claims 1, 5, 11, 12, and 31-34 are

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[4] Examiner's Answer mailed 7 November 2006 ("Ms.").

unpatentable § 102(b) as anticipated by Greenway 111 or Greenway IV, and (iii) claims 1-34 are unpatentable under § 103(a) as obvious over Kazuo.

III. Discussion

Appeal to the Board is from a decision of the Examiner, not from the reasons upon which such decision is based. Apparently, it is Appellant's position that whenever the Board sets forth a claim construction that was not expressed in the same words by the Examiner, it follows that the claim construction constitutes a new ground of rejection. We disagree.

The criterion of whether a rejection is considered "new" in a decision by the Board is whether Appellant has had a fair opportunity to react to the thrust of the rejection. *In re Kronig*, 539 F.2d 1300, 1303 (CCPA 1.976). Here, we agree with the Examiner's basis for rejecting (a) claims 1, 5, 9, 10, and 31-34 under 35 U.S.C. § 102(b) as anticipated by Kazuo, (b) claims 1, 5, 11, 12, and 31-34 under 35 U.S.C. § 102(b) as anticipated by Greenway III or Greenway IV, and (c) claims 1-34 under 35 U.S.C. § 103(a) as obvious over Kazuo. We also agree with the Examiner that Appellant has not provided sufficient evidence on this record to establish that the subject matter defined in claims 1-34 is patentable over the prior art. The Examiner reviewed Appellant's evidence, as did we (*see* BPAI Decision 12-16 and 18-20). The basic thrust of the rejection by the Examiner and the Board was the same, and we believe that Appellant has had a fair opportunity to react to those rejections.

In particular, the Examiner (FF 31-32) and the '596 patent specification (FF 25-26) both suggest that promoting lean body mass is not limited to increasing lean body mass, but also encompasses maintaining lean body mass while decreasing adipose tissue and that increasing lean body mass may further enhance promoting lean body mass. Indeed, the fact that the Examiner rejected claims 1 and 5 together under § 102(b) suggests that she deemed a method of promoting lean body mass (claim 1) and a method of shifting the proportion between lean body mass and adipose tissue in favor of lean body mass (claim 5) to be the same method discussed in the prior art, i.e., Kazuo and the Greenway references (FF 31). Moreover, the Examiner indicates in her discussion of the Greenway references that body mass is the sum of lean body mass plus body fat and, this, reduction of fat would translate into promotion of lean body mass (FF 32). Thus, it reasonably appears the Examiner broadly interpreted "promoting" lean body mass to not only include increasing lean body mass as argued by Appellant, but also to include reducing body fat relative to lean body mass. Therefore, it appears on its face that the Examiner and the Board were all construing "promoting" in a similar manner consistent with the '596 patent specification.

Therefore, we will not designate our affirmance as constituting a new ground of rejection under 37 C.F.R. § 41.50(b).

IV. Conclusion

Appellant's request for rehearing has been granted to the extent that the BPAI Decision on

Appeal mailed December 13, 2007 has been reconsidered in light of Appellant's arguments. However, the request is denied because we decline to modify the BPAI Decision in any respect.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a). *See* 37 C.F.R. §§ 1.550(c) and 41.52(b).

REHEARING DENIED

Rvb

ARENT FOX LLP
1050 Connecticut Avenue, N.W. Suite 400
Washington, DC 20036

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

2008-1257, 2009-1317
(Reexamination No. 90/007,327)

IN RE SAMI CHEMICALS AND EXTRACTS, LTD.

Appeals from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences.

ORDER

NOTE: This order is nonprecedential.

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

ORDER

A combined petition for panel rehearing and for rehearing en bane having been filed by the Appellant, and the petition for rehearing, having been referred to the panel that heard the appeal, and thereafter the petition for rehearing en bane having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for panel rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the petition for rehearing en banc be, and the same hereby is, DENIED.

The mandate of the court will issue on May 4, 2010.

FOR THE COURT,

Jan Horbaly
Clerk

Dated: 04/27/2010

cc: Richard J. Berman
Raymond T. Chen

IN RE SAMI CHEMICALS, 2008-1257, 2009-1317
JAN WOW
(PTO - 90/007,327)

35 U.S.C. 102
Conditions for patentability; novelty and loss of right to patent.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in - (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for

the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language; or

(f) he did not himself invent the subject matter sought to be patented, or

(g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. 103
Conditions for patentability; non-obvious subject matter.

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(b)

(1) Notwithstanding subsection (a), and upon timely election by the applicant for patent to proceed under this subsection, a biotechnological process using or resulting in a composition of matter that is novel under section 102 and nonobvious under subsection (a) of this section shall be considered nonobvious if-

(A) claims to the process and the composition of matter are contained in either the same application for patent or in separate applications having the same effective filing date; and

(B) the composition of matter, and the process at the time it was invented, were owned by the same person or subject to an obligation of assignment to the same person.

(2) A patent issued on a process under paragraph (1)-

(A) shall also contain the claims to the composition of matter used in or made by that process, or

(B) shall, if such composition of matter is claimed in another patent, be set to expire on the same date as such other patent, notwithstanding section 154.

(3) For purposes of paragraph (1), the term "biotechnological process" means

(A) a process of genetically altering or otherwise inducing a single or multi celled organism to-

(i) express an exogenous nucleotide sequence,

(ii) inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or

(iii) express a specific physiological characteristic not naturally associated with said organism;

(B) cell fusion procedures yielding a cell line that expresses a specific protein, such as a monoclonal antibody; and

(C) a method of using a product produced by a process defined by subparagraph (A) or (B), or a combination of subparagraphs (A) and (B).

(c)

(1) Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.

(2) For purposes of this subsection, subject matter developed by another person and a claimed invention shall be deemed to have been owned by the same

person or subject to an obligation of assignment to the same person if -

(A) the claimed invention was made by or on behalf of parties to a joint research agreement that was in effect on or before the date the claimed invention was made;

(B) the claimed invention was made as a result of activities undertaken within the scope of the joint research agreement; and

(C) the application for patent for the claimed invention discloses or is amended to disclose the names of the parties to the joint research agreement.

(3) For purposes of paragraph (2), the term "joint research agreement" means a written contract, grant, or cooperative agreement entered into by two or more persons or entities for the performance of experimental, developmental, or research work in the field of the claimed invention.

§ 41.50 Decisions and other actions by the Board.

(a) *Affirmance and reversal.* The Board may affirm or reverse an examiner's rejection in whole or in part. Affirmance of a rejection of a claim constitutes a general affirmance of the decision of the examiner on that claim, except as to any rejection specifically reversed.

(b) *Remand.* The Board may remand an application to the examiner. If in response to a remand for further consideration of a rejection, the examiner enters an examiner's answer, within two months the appellant shall exercise one of the following two options to avoid abandonment of the application or termination of a reexamination proceeding:

(1) *Request to reopen prosecution.* Request that prosecution be reopened before the examiner by filing a reply under § 1.111 of this title with or without amendment or submission of evidence. Any amendment or evidence must be responsive to the remand or issues discussed in the examiner's answer. A request that complies with this paragraph will be entered and the application or patent under reexamination will be reconsidered by the examiner under the provisions of §1.112 of this title. A request under this paragraph will be treated as a request to dismiss the appeal.

(2) *Request to re-docket the appeal.* The appellant may request that the Board re-docket the appeal (see §41.35(a) of this subpart) and file a reply brief as set forth in §41.41 of this subpart. A reply brief may not

be accompanied by any amendment or evidence. A reply brief which is accompanied by an amendment or evidence will be treated as a request to reopen prosecution pursuant to paragraph (b)(1) of this section.

(c) *Remand not final action.* Whenever a decision of the Board includes a remand, the decision shall not be considered a final decision of the Board. When appropriate, upon conclusion of proceedings on remand before the examiner, the Board may enter an order making its decision final.

(d) *New ground of rejection.* Should the Board have a basis not involved in the appeal for rejecting any pending claim, it may enter a new ground of rejection. A new ground of rejection shall be considered an interlocutory order and shall not be considered a final decision. If the Board enters a new ground of rejection, within two months appellant must exercise one of the following two options with respect to the new ground of rejection to avoid dismissal of the appeal as to any claim subject to the new ground of rejection:

(1) *Reopen prosecution.* Submit an amendment of the claims subject to a new ground of rejection or new evidence relating to the new ground of rejection or both, and request that the matter be reconsidered by the examiner. The application or reexamination proceeding on appeal will be remanded to the examiner. A new ground of rejection by the Board is binding on the examiner unless, in the opinion of the examiner, the amendment or new evidence overcomes the new ground of rejection. In the event

the examiner maintains the new ground of rejection, appellant may again appeal to the Board.

(2) *Request for rehearing.* Submit a request for rehearing pursuant to §41.52 of this sub-part relying on the Record.

(e) *Recommendation.* In its opinion In support of its decision, the Board may include a recommendation, explicitly designated as such, of how a claim on appeal may be amended to overcome a specific rejection. When the Board makes a recommendation, appellant may file an amendment or take other action consistent with the recommendation. An amendment or other action, otherwise complying with statutory patentability requirements, will overcome the specific rejection. An examiner, however, upon return of the application or reexamination proceeding to the jurisdiction of the examiner, may enter a new ground of rejection of a claim amended in conformity with a recommendation, when appropriate.

(f) *Request for briefing and information.* The Board may enter an order requiring appellant to brief matters or supply information or both that the Board believes would assist in deciding the appeal. Appellant will be given a non-extendable time period within which to respond to the order. Failure of appellant to timely respond to the order may result in dismissal of the appeal in whole or in part.

(g) *Extension of time to take action.* A re-quest for an extension of time to respond to a request for briefing and information under paragraph (b) of this section is not authorized. A request for an extension of time to respond to Board action under paragraphs

(b) and (d) of this section shall be presented as a petition under §41.3 of this part.

United States Patent Patent Number: 5,804,596
Majeed , et al. Date of Patent: Sep. 8, 1998

METHOD OF PREPARING A FORSKOHLIN COMPOSITION FROM FORSKOHLIN EXTRACT AND USE OF FORSKOHLIN FOR PROMOTING LEAN BODY MASS AND TREATING MOOD DISORDERS

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Appl. No.: **08/807,652**

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Intl. Cl...... **A61K 31/55**
U.S. Cl...... **514/455**
Field of Search..... 514/455

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Allen, et al., *The Journal of Pharmacology and Experimental Therapeutics*, vol. 238, Not. 2, pp. 659-664, "Relationships between cyclic AMP Levels and Lipolysis in Fat Cells After . . .".

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Wachtel, et al, *Psychopharmacology* (1986) 90 pp. 430-435, "Effects of forskolin and cyclic nucleotides in animal models predictive of antidepressant activity: interactions with rolipram".

Primary Examiner: Goldberg; Jerome D.
Attorney, Agent or Firm: Nikaido Marmelstein Murray & Oram LLP

ABSTRACT

A method of promoting lean body mass in an individual is disclosed, comprising administering to the individual a lean body mass promoting effective amount of forskohlin. A method of treating a mood disorder is also disclosed, comprising administering to a patient in need thereof a mood disorder treating effective amount of forskohlin. Compositions suitable for promoting lean body mass and/or treating a mood disorder are also disclosed, the composition comprising about 1 to about 40% forskohlin in combination with at least one physiologically acceptable carrier or excipient. A method of preparing a forskohlin composition from a forskohlin extract of Coleus Forskoli plant is further disclosed, as well as a forskohlin composition prepared by the method.

8 Claims, No Drawings

METHOD OF PREPARING A FORSKOHLIN COMPOSITION FROM FORSKOHLIN EXTRACT AND USE OF FORSKOHLIN FOR PROMOTING LEAN BODY MASS AND TREATING MOOD DISORDERS

BACKGROUND OF THE INVENTION

Most weight loss pharmaceutical compositions and nutraceutical aids are designed to decrease the amount of body fat in an individual by decreasing the individual's appetite for food, decreasing the amount of food absorption in the individual, slowing down the rate of fatty acid synthesis within the body, or increasing the rate of catabolism of fatty acids. The following are some examples of weight loss products and their mechanisms. Dexfenfluramine increases the brain levels of serotonin, a neurotransmitter and neurohormone that quells the appetite. Sibutramine also increases the levels of serotonin, as well as noradrenaline, and works to quell the appetite. Neuropeptide Y inhibitors curb the appetite, as well as stimulating the body to burn more sugars and less fat. Bromeriptine mimics the neurotransmitter dopamine, and may reduce blood sugar and fat production by the liver. Leptin, a hormone generated by adipocytes, affects the hypothalamus. Cholecystokinin, a hormone and neurotransmitter, acts to reduce appetite. Butabindide blocks an enzyme that inactivates cholecystokinin. Orlistat interferes with pancreatic lipase, which results in poor absorption of dietary fat. Insulinotropin is a glucagon-like hormone which prevents obesity by slowing down the emptying of the stomach. Bta-243 stimulates beta-adrenergic receptors on adipocytes, with a resulting increase in

the burning of fatty acids. Troglitazone is a synthetic hormone which signals muscle cells to utilize fat for energy, rather than sugars. Cytokine regulators change the activity of hormone-like cytokines and alter the communication among cells, resulting in weight loss. Hydroxycitric acid acts as an inhibitor of enzyme citrate lyase, which subsequently slows down the synthesis of fatty acids and increases the rate at which fatty acids are burned.

The average amount of body fat in the American male is 22 to 25%, and in the American female, the average amount of fat is 33 to 35%. These values are far above optimal values, which are 15 to 19% for 20-29 year old males and 19 to 23% for 20-29 year old females. Corresponding values for 40-49 year olds are 17 to 21% and 21 to 25%, respectively; and for 60 year olds, the corresponding values are 19 to 23% and 23 to 27%, respectively. In highly overweight individuals, fat tissue can constitute up to 70% of body weight.

The remaining percentage of body composition corresponds to the lean body mass. Lean body mass is composed of muscle, vital organs, bone, connective and other non-fatty tissues in the body, and most of the body water. The body's metabolic rate is in direct proportion to the amount of lean body mass. Therefore, considering the lean body mass is important for any weight loss strategy.

The aforementioned weight control means do not take into account the importance of maintaining or increasing the lean body mass in the process of weight loss. In fact, regimens to decrease body fat often contribute to the catabolic wasting of lean body mass. Increased lean body mass regulates body

metabolism and helps in losing weight, as well as maintaining the accomplished weight reduction. On the other hand, diminished lean body mass slows down body metabolism and results in difficulties in maintaining an appropriate, healthy body weight. Thus, an ideal weight management approach should be to reduce body weight to acceptable levels by restoring the optimal proportions of fat to lean body mass. By maintaining or increasing the lean body mass while simultaneously reducing body fat, the weight loss regimen would serve the general purpose of improving the overall health of the individual.

Maintaining or increasing the lean body mass (for example, skeletal muscles) is one of the important considerations for any weight loss strategy because lean body mass determines the rate of metabolism and the body's thermogenic response to food, and food induced thermogenesis and the metabolic rate, in turn, control body weight by an increase in the catabolism of body fat. This is so because thermogenesis is preferentially fueled by fatty acids derived from stores of body fat and from food. In addition, a high rate of thermogenesis contributes to more food being absorbed and to the preferential build-up of lean body mass, rather than adipose tissue.

It is well known in the literature that forskohlin is related to lipolysis in isolated fat cells in vitro. See, for example, *Horm. metabol. Res.* 19 (1987), pp. 358-360; *J. Pharmacology and Experim. Therapeutics* 238 (1986), pp. 659-664; *J. Pharmacology and Experim. Therapeutics* 244 (1988), pp. 852-858. The biological mechanism for this action seems to be that forskohlin increases the

levels of cyclic AMP (cAMP) or exerts action similar to cAMP. The following other biological effects of forskohlin have been described as a result of the cAMP or cAMP-like mechanisms: inhibition of platelet aggregation, increased chronotropic and inotropic effect on the heart, hypotensive action, bronchodilating action, potentiation of insulin secretion, increased synthesis of body steroids, increased release of adrenocorticotropic hormone (ACTH) and decreased intraocular pressure. However, the use of forskohlin for the promotion of lean body mass has not been reported.

Forskohlin has also been shown to be effective for reversing hypothermia or hypokinesia in mice depleted of presynaptic endogenous monoamines by pretreatment with reserpine, α-methyl-p-tyrosine and p-chlorophenylalanine, when the forskohlin is co-administered with cyclic nucleotide analogs dibutyryl cAMP (dBcAMP), 8-bromo cAMP (8-BrcAMP) and dibutyryl cGMP (dBcGMP). See *Psychopharmacology* 90 (1986), pp. 430-435. The authors of this study noted that antagonism of reserpine-induced hypothermia and hypokinesia are regarded as classic tests for predictions of possible clinical antidepressant activity. However, no reports exist showing that forskohlin can be effective in treating mood disorders such as depression and anxiety in humans. Such mood disorders are damaging in their own respects to the health of the individual, but also can, in some cases, lead to overeating and secondary obesity which further damages the health of the individual. Thus, a health regimen should also require that the individual be emotionally stable and highly motivated.

The present inventors know of no published or patented method of preparing a forskohlin composition from a forskohlin extract of the *Coleus Forskohli* plant. Such a method would be useful for providing a more pure form of forskohlin than that which is presently available on the market, and for providing a standardized amount of active forskohlin, which can thereafter be further processed by other manufacturers, or combined with nutritional supplements by end users.

SUMMARY OF THE INVENTION

The present invention relates to a method of promoting lean body mass in an individual, comprising administering to the individual a lean body mass promoting effective amount of forskohlin.

Further subject matter of the invention is a method of treating a mood disorder in a patient in need of such treatment, comprising administering to the patient a mood disorder treating effective amount of forskohlin. The mood disorder can be, for example, depression or anxiety.

The present invention also relates to a composition comprising an amount of forskohlin in combination with a physiologically acceptable carrier or excipient.

Yet another subject matter of the invention is a method of preparing a forskohlin composition from a forskohlin extract of *Coleus Forskohli* plant, comprising:

(a) providing a forskohlin extract of *Coleus Forskohli* plant;

(b) dissolving the forskohlin extract in a first solvent;

(c) thereafter separating an amount of forskohlin from an amount of impurities in a step comprising combining the product produced in step (b) with a second solvent, wherein the amount of forskohlin is insoluble in the second solvent and the amount of impurities are soluble in the second solvent; and

(d) preparing a forskohlin composition by combining the amount of forskohlin obtained in step (c) with at least one physiologically acceptable carrier or excipient to produce a forskohlin composition having a predetermined forskohlin content.

The present invention also includes compositions prepared from the above method, as well as methods of promoting lean body mass and treating mood disorders using the compositions thus prepared.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention shifts the proportion between lean body mass and adipose tissue in favor of lean body mass in order to restore the ideal physiological proportions between lean and fat body mass, thus improving the overall health status of the individual. The positive health effect of the invention can be measured by decreases in the waist hip ratio (WHR) and the body mass index (BMI), both good predictors of morbidity and mortality.

Without being bound by any theory, the present inventors believe that the invention increases the lean body mass by stimulating the enzyme adenylate cyclase (AC), with a resulting increase in the levels of cAMP. The increase levels of cAMP in the tissues correspond well to enhancing the thermogenic

response to food. An increase in the thermogenic response to food, in turn, improves absorption of nutrients and their preferential incorporation into lean body mass. Thus, the formation of lean body mass is promoted.

Again without being bound by any theory, the present inventors believe that the mechanism of the invention specifically works as follows:

forskohlin stimulates noradrenaline released from the sympathetic nerves to interact with beta-adrenergic receptors;

this results in an increase in AC enzyme, with a subsequent rise in cAMP levels;

cAMP stimulates the activity of a protein kinase which phosphorylates a hormone-sensitive lipase to produce the active form of this enzyme;

the lipase stimulates the release of fatty acids from body adipose depots;

the released fatty acids stimulate the uncoupling process in the mitochondria, resulting in thermogenesis and provision of fuel to increase thermogenesis;

there is an increase in T4 5' deiodinase, which activates the thermogenic thyroid hormone T3;

there is an increase in the beta-adrenergic dependent metabolic functions, which leads to an increase in the lean body mass, i.e., activation of phosphorylase in skeletal muscles, insulin secretion, and the synthesis and secretion of anabolic steroid hormones.

Regarding the control of mood disorders, without being bound by any theory, the present inventors

believe that the biological mechanism by which forskohlin treats these disorders is as follows:

forskohlin restores the level of monoamines for presynaptic availability, which has known anti-depressant action;

there is an increase in cAMP in the postsynaptic effector cells in the brain, which is a "second messenger", in comparison to the "primary messenger" action of the monoamines.

In the present method of promoting lean body mass, the forskohlin should be administered in a daily dose of from about 10 to about 60 mg. It is preferred that the daily dose be divided into a plurality of individual doses. It is further preferred that three individual doses be used. In any case, the individual doses are preferably from about 10 to about 20 mg each.

In the present method of treating a mood disorder, the forskohlin should be administered in a daily dose of from about 10 to about 60 mg. It is preferred that the daily dose be divided into a plurality of individual doses. It is further preferred that three individual doses be used. In any case, the individual doses are preferably from about 10 to about 20 mg each.

In either method of the invention, the forskohlin can be administered in combination therapy with additional ingredients. Some examples of additional ingredients are extract from *Garcinia gambogia* in the form of natural (-) hydroxycitric acid or its salts (e.g., calcium or potassium salts); organic salts of vanadium (e.g., bis maltolato vanadium or bis glycinato vanadium); extract from *Piper nigrum* (black pepper) or *Piper longum* (long pepper)

containing alkaloid piperine; or extract from *Sida cordifolia* containing alkaloid ephedrine.

The forskohlin can be administered orally, topically or parenterally, although orally is preferred. Carriers, diluents or excipients are well known in the art.

The present invention includes forskohlin compositions. The composition can comprise about 1 to about 40% forskohlin. It is more preferred to include about 5 to about 20% forskohlin. It is even more preferred to include about 8 to about 15% forskohlin. A composition containing about 10% forskohlin is most preferred.

The present invention also includes a method of preparing a forskohlin composition from a forskohlin extract of *Coleus Forskohli* plant, comprising:

(a) providing a forskohlin extract of *Coleus Forskohli* plant;

(b) dissolving the forskohlin extract in a first solvent;

(c) thereafter separating an amount of forskohlin from an amount of impurities in a step comprising combining the product produced in step (b) with a second solvent, wherein the amount of forskohlin is insoluble in the second solvent and the amount of impurities are soluble in the second solvent; and

(d) preparing a forskohlin composition by combining the amount of forskohlin obtained in step (c) with at least one physiologically acceptable carrier or excipient to produce a forskohlin composition having a predetermined forskohlin content.

Step (a) of the method includes providing a forskohlin extract of the *Coleus Forskohli* plant. The extract can be obtained in a number of ways, however, the present inventors have devised a preferred method of obtaining the extract.

The content of forskohlin in the plant varies substantially with location, climatic conditions, mode of irrigation and age of the plant. The content usually is between 0.1 to 0.5%. The roots of the plant are washed with water, dried and powdered. A large amount (for example, about 100 kgs) of powdered plant root is subjected to extraction in order to get an appreciable yield of extract.

The roots are subjected to extraction using a suitable solvent. Examples of suitable solvents include toluene, methanol, ethanol, chloroform, ethylacetate, ethylenedichloride, and the like. A mixture of toluene and methanol in a ratio of about 100:1 to about 100:2 is preferred. A ratio of about 100:1 is most preferred.

The volume of solvent mixture and the number of extraction cycles are determined based on the type of extractor used. Normally, about 10 volumes of the solvent mixture are preferred in a continuous-type solvent extractor or Soxhlet extractor.

Ideally, the extraction is performed at a temperature ranging from about 35° to 105°C. The preferred temperature is between about 60° to about 75° C. Extraction time is usually about 6 hours. The efficiency of the extraction is increased when the extraction is performed with pressure, for example, 1 kilo.

After the extraction has been performed a number of times to give an appreciable yield, the extracts are combined, filtered and concentrated under vacuum at low temperatures, preferably at less than 60°C. The use of a thin film evaporator, rotary film evaporator or agitated wiped film evaporator is preferred for concentrating the extract in order to avoid decomposition of the forskohlin, which is temperature sensitive. After the solvent is removed from the system, an extract is obtained in the form of a paste.

Step (b) of the method provides that the forskohlin extract is dissolved in a first solvent. Any of the solvents used in the extraction of the forskohlin can be used at this stage, e.g. toluene, methanol, ethanol, chloroform, ethylacetate, ethylenedichloride, and the like. Toluene is preferred. The paste is dissolved in a minimum amount of the first solvent.

Step (c) of the method includes separating an amount of forskohlin from an amount of impurities. This separating step includes combining the dissolved extract/first solvent produced in step (b) with a second solvent. The forskohlin is insoluble in the second solvent and the impurities are soluble in the second solvent. Thus, the impurities remain in solution, while the forskohlin separates out of the second solvent.

Any solvent in which forskohlin is insoluble can be used as the second solvent. It is preferred, however, that a solvent is chosen in which a large amount of impurities associated with the extract are soluble, so that the resultant forskohlin obtained in this step is substantially more pure than it was in

extract form. Petroleum ether (having a boiling point in the range of 60° to 80°C) is most preferred.

The second solvent is preferably combined with the dissolved extract/first solvent produced in step (b) at a ratio of first solvent to second solvent ranging from about 1:10 to about 1:20. A ratio of about 1:20 is more preferred. Preferably, the resultant mixture is agitated at a temperature ranging from 40° to 60°C for a few hours, preferably about 2 hours. Forskohlin is insoluble at this temperature and at this solvent ratio.

The forskohlin is thereafter collected (for example, via filtration) and preferably again dissolved in a minimum quantity of first solvent. The second solvent is thereafter added, this time preferably in a ratio of first solvent to second solvent of about 1:25. The resultant mixture is thereafter preferably again agitated at a temperature ranging from 40° to 60°C for a few hours, preferably about 2 hours. The insoluble product is again collected, and the process may be repeated several times in order to obtain forskohlin of the required purity.

Normally, the purification process described above is performed three times to obtain a product containing about 15 to about 20% forskohlin, which is usually sufficient for most purposes, although higher purities are certainly well within the skill of an ordinary worker. The product preferably contains from about 15 to about 40% forskohlin, although the process of the invention is unique in that it can provide 100% pure forskohlin. The remainder of the product is organic material from the *Coleus Forskohli* plant. The yield is usually about 1.5 kgs of product for every 100 kgs of *Coleus Forskohli* root.

The product obtained in step (c) is normally hygroscopic, and not convenient to use as such. Therefore, step (d) of the present method includes preparing a forskohlin composition by combining this product with at least one physiologically acceptable carrier or excipient to produce a forskohlin composition having a predetermined forskohlin content. Preferable excipients are, for example, magnesium oxide, magnesium carbonate, dicalcium phosphate, and the like. The quantity of excipients used is, of course, based on the predetermined forskohlin content. Standardization of about 1 to about 40% forskohlin is normally achieved, however, depending on the specific need, this product can be upgraded to contain up to 100% forskohlin. This is accomplished by a column chromatography technique, followed by re-crystallization. Preferred standardization is to about 5 to about 20% forskohlin, more preferred about 8 to about 15%, most preferably about 10%.

The forskohlin compositions prepared by the above method are stable. The stability of the compositions has been determined by subjecting the compositions to normal ambient storage conditions, as well as to accelerated storage conditions. During this study, the quality has been tested for stability indicating parameters. As per the study, the extract is stable for a period of not less than 5 years, when it is stored under normal ambient storage conditions.

The present invention includes products (i.e., compositions) produced by this method. The products can usually contain about 1 to about 40% forskohlin, although up to 100% pure forskohlin is possible. Preferred amounts are about 5 to about 20%

forskohlin, more preferred about 8 to about 15%, most preferably about 10%.

The present invention also includes methods of promoting lean body mass and methods of treating a mood disorder using the compositions produced by the above-referenced method. Similar dosage levels are effective as those used for conventional forskohlin compositions.

The specifications of an example forskohlin composition prepared according to the described method are as follows:

Description	brown powder with a characteristic odor
Identification	to comply with standard by thin layer chromatography
Loss on Drying	not more than 10.0%
Solubility in Water	insoluble
Solubility in Alcohol	not less than 45.0%
Heavy Metals	not more than 20 ppm
Arsenic	not more than 1 ppm
Lead	not more than 4 ppm
Bulk Density	between 0.4 and 0.7 g/mL
Sieve Test	not less than 100.0% passes through 20 mesh not less than 75.0% passes through 40 mesh not less than 50.0% passes through 80 mesh
Content of Forskohlin	not less than 10.0% and not more than 11.0% by HPLC

Reasonable modifications of the inventions disclosed herein are well within the scope of those skilled in the art, and are also intended to be within

the scope of the present invention. The scope of the present invention is not intended to be limited by the specific examples set out herein, but rather is to be interpreted according to the following claims.

We claim:

1. A method of promoting lean body mass in a human individual in need thereof, comprising administering to the individual a lean body mass promoting effective amount of forskohlin.

2. The method of claim 1, wherein the forskohlin is administered in a daily dose of about 10 to about 60 mg.

3. The method of claim 2, wherein the daily dose is divided into a plurality of individual doses.

4. The method of claim 1, wherein the forskohlin is administered in an individual dose of about 10 to about 20 mg.

5. A method of shifting the proportion between lean body mass and adipose tissue in favor of lean body mass in a human individual in need thereof, comprising administering to the individual a proportion shifting effective amount of forskohlin.

6. The method of claim 5, wherein the forskohlin is administered in a daily dose of about 10 to about 60 mg.

7. The method of claim 6, wherein the daily dose is divided into a plurality of individual doses.

8. The method of claim 5, wherein the forskohlin is administered in an individual dose of about 10 to about 20 mg.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO.	: 5,804,596	Page 1 of 1
APPLICATION NO.	: 081807652	
DATED	: September 8,1998	
INVENTOR(S)	: Muhammed Majeed et al	

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page -

Item [75], Inventors, please correct the second inventor's name from "**Vladimir Badmaey**" to -- **Vladimir Badmaev** --.

Signed and Sealed this
Fifth Day of September, 2006

JON W. DUDAS
Director of the United States Patent and Trademark Office

PTO: 2005-5621

Japanese Published Unexamined Patent Application (A) No. 06-133731, published May 17, 1994; Application Filing No. 04-309500, filed October 23, 1992; Inventor(s): Kazuo Mitsumura; Assignee: Zenex Corporation; Japanese Title: Diet Food

DIET FOOD

CLAIM(S)

Diet food containing forskohlin and its related compound.

DETAILED DESCRIPTION OF THE INVENTION

(0001)

(Field of Industrial Application)

The present invention pertains to one type of diet food.

(0002)

(Prior Art)

Many types of diet food have been developed in the past in order to prevent obesity caused by excessive calorie intake. Among them, there is one type, which is low calorie food, such as food with reduced fat and a jam using an artificial sweetener, and another type is the food that uses a component of konnyaku to prevent other food from being absorbed into a body. [T. Note: There is no English equivalent to the term "konnyaku"; one English equivalent I came across in the past is "devil's tongue," although I suspect the authenticity of the rendition, for it does not communicate any meaning.

I, as a native Japanese, know that this product is prepared by drying and pulverizing a specific type of vegetable and making the powder into a gelatin form. I will use the word "konnyaku as is in this context].

(0003)

(Problems of the Prior Art to Be Addressed)

However, it is monotonous to always eat low-calorie food and sweetness-reduced food to prevent excessive intake of calorie, and replacing a sweetener with an artificial one is not possible when dining out. Accordingly, by these conventional methods, a definite diet effect could not be expected. With the method to take the food that can prevent the nutrients of other food from being absorbed, intake of all the nutrients is prevented. If such a type of food is taken too much, it may result in lack of necessary nutrition, which is dangerous. The present invention attempts to present an effective diet food that can prevent fat from being stored in a body while eating freely to take the necessary nutrients.

(0004)

(Means to Solve the Problems)

The diet food of the present invention contains forskolii extract as its component.

(0005)

(Operation)

The diet food of the present invention contains a forskohlii extract extracted from the root or its powder of Coleus forskohlii by using water or

alcohol, which belongs to a Lamiaceae variety, more specifically, the diet food contains forskohlii and the similar compound. Forskohlii taken in an animal body in form of food is recognized as having a function to activate adenylcyclase (cAMP synthesis enzyme) in cells. Once the adenylcyclase is activated, cyclic adenosine monophosphate (cAMP) is increased, by which protein kinase and hormone-sensitive lipase are activated. Then, the forskohlii decomposes the fat into glycerol and fatty acid, and moves out of the cell. Thus, forskohlin has affinity with fat cell and selectively promotes a lipid metabolism. Therefore, forskohlin presumed to produce an effect of diet.

(0006)

(Embodiment Example)

A forskohlii extract is extracted from the root of Coleus forskohlin of Larniaceae variety naturally growing in India and Nepal (Fig. 1). The fact that this extract contains forskohlin and the similar compound has been confirmed by thin layer-chromatography and high-speed liquid chromatography. It has been also confirmed by bioassay Using a rat's femoral artery smooth muscle that this forskohlii extract has 1116th activity of that of reference substance, forskolin [made by Wako Pharmaceutical, Inc.). Subsequently, the experiment conducted to confirm the diet effect of forskohlii extract is explained below.

(0007)

Experiment 1

Forskohlii extract's effect on reduction of rat's body weight and on improving lipid metabolism in blood

Experiment Method

Five week old Sprague Dawley male rats (body weight 116 ± 5 g) were raised in an individual cage under the conditions: room temperature 25 ± 2°C, humidity 50 ± 20°C, illumination 7: 00 - 18:00, and they were used for experiment. After one week of preliminary raising, the rats with no abnormality are divided into a first group of 6 rats and a second group of 6 rats. To a powdered rat feed (CE = 2 by Nippon Clare, Inc.), cholesterol 1% and sodium chorate 0.25% were added to prepare a high fat food. This was fed to the first group of rats and the feed prepared by adding forskohlii extract 1% to the aforementioned high fat good was fed to the second group of rats for comparison.

(0008)

The feed 20 g was fed to one rat per a day, and the remaining portion was measured to find the amount the rat has eaten. The effect of the feeding for one week was measured at the end of first week and at the end of the second week by the following equation (1). At the end of raising period of two weeks, the body weight was measured and an increase in weight was measured likewise by the following equation (2). Subsequently, no food was given for 10 hours. Then, blood was collected by inserting a needle into the heart to collect the blood

serum. By an O-phthalaldehyde method (Wako Pharmaceutical, Inc.), the total cholesterol value was measured, and by Pepalin Mangan Method (kit made by Wako Pharmaceutical, Inc.), HDL cholesterol value was measured. Also, triglyceride was measured by an enzyme method (kit made by Nippon Shoji, Inc.). The aforementioned equations are as follows.

Feed efficiency(%) = {(weight at the end of the week — weight at the start of the week)/the amount of feed eaten} x 100...(1).

Weight increase rate(%) = (weight after 2 weeks — initial weight) x 100...(2).

By the forskohlii extract feeding, the increase of weight was prevented. In addition, the total cholesterol value in blood serum and triglyceride value were reduced, and the HDL cholesterol value was increased. In other words, the lipid metabolism in blood was improved. From the above result, it was confirmed that a forskohlii extract has the functions of preventing the increase of body weight and of improving lipid metabolism.

Table 1

	First group (fed high fat food)	Second group (fed forskohlii extract)
Weight increase rate (%)	120 + 14	107 + 17
Feed efficiency (%)	First week 32 ± 3 Second week 48 ± 5	30 ±4 37 ± 5

Total cholesterol value in serum (mg/dl)	227 ± 60	181 ± 5
HDL cholesterol value (mg/dl)	22 ± 4	29 ± 5
Triglyceride (mg/dl)	126 ± 19	112 ± 21

(0010)

Experiment 2

Effect of forskohlii extract on preventing human body weight increase

Experiment Method

Seven female volunteers who are 20 — 40 years old and in good health were subjected to the experiment. The forskohlii extract 500 g which was the same extract as that used in the aforementioned experiment was mixed with 2 kg of lactose, and 300 mg of this mixture was formed into one tablet. These healthy volunteers took 3 tablets containing the forskolii extract 3 times a day before meal while continuing a normal meal.

Result of Experiment

As shown in Table 2, it was observed that 6 out of 7 volunteers had a weight loss of 4 - 1 kg after taking forskohlii extract for 2 weeks.

Table 2

Volunteers (age)	Initial weight (kg)	Weight after 2 weeks (kg)
1 (41)	62	59
2 (29)	53	51
3 (25)	57	57
4 (45)	49	45
5 (27)	44	43
6 (20)	48	47
7 (32)	55	53

(0011)

By this, the forskohlii extract was recognized to be effective for prevention of obesity and for prevention of high cholesterol. As a result of experimenting the forskohlii extract on guinea pigs, dogs, and rats, it was recognized that use of 10 — 1,000 μg/kg of forskohlii extract is effective for lowering blood pressure. Therefore, if the forskohlii extract is used for food for diet, it is preferably added to the food which cannot be taken by a large amount, e.g., carbon drinks, coffee, spray food.

(0012)

(Advantage)

By taking the diet food of the present invention, one can prevent the fat accumulation in one's body while eating normally and taking necessary nutrition.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows steps of extracting the forskohlii extract.

FIGURE OMITTED FOR PRINTING

Translations
U. S. Patent and Trademark Office
8/25/05
Akiko Smith

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Regional Fat Loss from the Thigh in Obese Women after Adrenergic Modulation

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ABSTRACT

Beta-adrenergic stimulation and alpha $_2$-adrenergic inhibition increase lipolysis from fat cells. Twenty-eight obese women were placed on a caloric-restricted diet and one of five treatments was applied to one thigh three to five times per week for four weeks: (1) isoproterenol injections; (2) cream containing colforsin (forskolin), aminophylline, and yohimbine; (3) yohimbine cream; (4) colforsin cream; or (5) aminophylline cream. The opposite thigh was treated with a placebo (injection or cream). The treated thighs lost significantly more girth after treatment, both by injection and by cream. No adverse reactions were attributable to either the cream or the injections. It is concluded that local fat reduction from the thigh can be safely accomplished.

INTRODUCTION

Fat is lost more rapidly from the abdomen than from the thigh after intestinal bypass surgery.[1] Studies of fat cells have shown that beta-adrenergic agonists

can directly increase cyclic adenosine monophosphate levels and stimulate lipolysis. There is a regional difference in this responsiveness to beta-agonists.[2] Fat cells from the abdomen are more sensitive to the lipolytic effects of beta-adrenergic stimulation than are those from the thigh. This appears to be because there are more $alpha_2$-receptors on fat cells of the thigh than of the abdomen.[3,4] Raising the norepinephrine concentration in the medium suspending the fat cells from the thigh increases in vitro lipolysis from these cells.[2] The maximal lipolytic rate in fat cells from the two locations is equal, but higher concentrations of norepinephrine are needed to reach that maximum when fat cells from the thigh are used. Blocking the $alpha_2$-receptors on fat cells from the thigh enhances lipolysis in the presence of norepinephrine.[2,4]

We hypothesized that by increasing the local concentration of beta agonists or by inhibiting phosphodiesterase or $Alpha_2$-adrenergic receptors to fat cells in the thigh, fatty acids could be released more readily. We report the results of a series of small trials to test this hypothesis.

MATERIALS AND METHODS

Study 1

Five women who were more than 20% above their desirable body weight (mean weight, 209 lb) and wished to lose weight from their thighs were recruited and placed on a diet of 600 kcal daily and encouraged to engage in a walking program. They received injections of 0.2 ml of 10^{-5} mol/L isoproterenol at intervals of 4 cm around the circumference of one thigh, two thirds of the way

from the knee to the greater trochanter, three days per week for four weeks. The 4-cm interval was chosen because calculations from the area of vasodilation on the skin suggested that the spheres of diffusion would overlap when this distance was kept. The opposite thigh was treated similarly, but using normal saline in a double-blind design.

Study 2

Five women (mean weight, 182 lb) who were more than 20% above desirable body weight and wished to lose weight from their thighs were recruited and placed on a diet of 600 kcal daily and encouraged to engage in a walking program. They were seen five days a week for four weeks. At each visit, warm wraps of 600 to 900 mosm/L of magnesium sulfate solution were applied to each thigh for 30 minutes, followed by an application of cream and plastic wrap. The cream applied to one thigh contained 1.2 X 10^{-5}mol/L colforsin (forskolin), 2.5 X 10^{-5}mol/L yohimbine, and 1. 3 X 10^{-2} mol/L aminophylline in xipamide (aquaphor) base. The other thigh received xipamide base only in a double-blind design.

Study 3

Eighteen women (mean weight, 197 lb) who were more than 20% above desirable body weight and wished to lose weight from the thighs were recruited and placed on a liquid formula diet of 800 kcal daily and encouraged to engage in a walking program. They were seen five days per week for four weeks. At each visit, warm wraps of 600 to 900 mosm/L of magnesium sulfate solution were applied to each thigh for 30 minutes, followed by cream application.

One thigh was treated in each patient with one of the three creams in xipamide: colforsin, 25 X 10^{-5} mol/L (six patients); yohimbine, 5 X 10^{-4} mol/L (six patients); or aminophylline, 1.3 X 10^{-2} mol/L (six patients). The other thigh in each subject was treated with xipamide only, in a double-blind design.

In each study, treatment effectiveness was judged by measuring the thigh circumference two thirds of the way from the knee to the greater trochanter, using the saline- or xipamide-treated thigh as the control. Differences were compared with Student's t test for paired observations.

RESULTS

In Study 1, all five women completed the four weeks of treatment and all but one lost weight. The four subjects who lost weight lost more girth from the thigh treated with isoproterenol injections than from the control thigh. In the total group, the thighs treated with isoproterenol lost a mean of 1.8 ± 0.89 cm more than the control thighs ($P < 0.05$). No changes in pulse rate, blood pressure, or other clinical parameters were noted.

In Study 2, all five women completed the four weeks of treatment and all but one lost weight. The five subjects lost a mean of 2.03 ± 1.36 cm more from the thighs treated with cream containing colforsin, yohimbine, and aminophylline than from the control thighs ($P < 0.05$). The only adverse effect was a pruritic rash that occurred on both thighs in one subject, which was judged to be related to the occlusive plastic-wrap dressing.